Dispersion Mapping Capabilities for Clinical Practice (Literature Review)

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Contents

The review includes a brief description of a new method in the electrocardiographic diagnostics, *viz*., Dispersion Mapping, and the main results of clinical studies. The general theoretical prerequisites and methodological aspects of application of the method were considered and the basic principles of analysis were depicted. The results of our original studies were stated. The data on diagnostic and prognostic meaning of the dispersion mapping in health groups and group of patients with different forms of the CHD, were heavily emphasized. Some distant outcomes of the acute coronary syndrome and results of other recent clinical studies were considered.

Introduction

Today, electrocardiology is still a fast-developing field of science and clinical practice. Widening the range of diagnostics tasks, which could be resolved, using some ECG methods of functional diagnostics, is the most important trend of its modern stage of development. They are being developed based on the recent achievements of the electrophysiology, biophysics, informatics, mathematical simulation, and computer technology *[31]*. The knowledge and experience in diagnostics of some physiological and pathological conditions using fundamentally new diagnostic approaches are being accumulated continuously. In the modern computer electrocardiographic systems, a more biophysically well-grounded approach to cardioelectrical potential parametrization is used, which requires special transformation of the measured derivation signals based on additional data on the physical structures of heart and body *[27]*, *[45]*, *[49]*, *[73]*, *[74]*, *[93]*, *[100]*, *[101]*. The mathematical models with integration of known medical logic principles and biophysical data in the unified algorithmic diagram are used.

There is a variety of the new technologies that are not only promising for the future, but even today find application in the routine clinical practice to detect the myocardial ischemia and estimate a disturbance in the myocardial electrical properties. When analyzing the ECG signal, besides detecting arrhythmia and measuring the ST-segment displacement, other electrophysiological variables can be measured. The analysis methods of such variables includes: the TWA (T-Wave Alternans), dispersion of Q-T and QRS intervals, T-Wave dispersion, signal-averaged analysis, dispersion mapping (DM), heart rate turbulence, *etc*. *[31]*, *[40]*, *[45]*.

At the present time, the well sufficient data on the informativity of the DM method upon screening have been collected *[17]*, *[19]*, *[23]*, *[28]*, *[74]*, *[102]* to diagnosticate different disturbances in the myocardial electrical properties, including those appeared during different ishemic changes of myocard *[34]*, *[37]*, *[44]*, *[88]*, *[91]*. The reasonability of these approaches is based on the concept of that the electrophysiological alteration of cells and their membranes is associated with remodeling after the ischemia episode or old myocardial infarction and that it is involved in arrhythmogenesis and in the progress of the “electromechanical disharmony” within the myocardial disfunction areas. This concept is confirmed by the found connection of the intensity of free radical proceses with DM indices *[13]* and ECG of high resolution indices *[15]*. While reflecting the electrical remodelling, the DM method is a sensitive, but not specific indicator of pathological processes occurring at the level of cell membranes, of the myocard-affecting factors, and disturbance reasons of microalteration characteristics. The DM indices reflect first of all the metabolic disorders due to the changes in the coronary microcirculation, microvascular resistance, and collateral circulation, and, to a less degree, the severity of epicardial arterial occlusion and partial perfusion heterogeneity, compensatory mechanisms of the myocardial blood flow and their deterioration, which lead to changes in the myocardial electrophysiological properties. In addition, it has been shown that consideration of the wave-like dynamics of DM indices is important upon monitoring in both healthy persons and patients having the myocardial pathology *[46]*.

This review presents some results of recent studies. The use of the new analysis method of changes in the myocardial electrophysiological properties seems to be an important aspect to improve the assess of the myocard ischemic damage severity, to prognosticate the course of CHD, to determine the indications for the preventive “aggressive” therapy, and to estimate its effectiveness in patients with CHD and myocard electric instability and variety of other important cardiological tasks.

Electrophysiological Fundamentals of Dispersion Mapping

The ECG Dispersion Mapping (ECG DM) is based on the computer formation of a map of the electric micro-alterations of the ECG signal. The analysis of the ECG microvibrations whose amplitude begins to alter on approaching to the points of the myocard functional stability loss forms the basis for the method. Even in the healthy heart, the periodical processes of the myocardial de- and re-polarization upon each cardiac beat have insignificant alterations, which are reflected by the low-amplitude vibrations of the ECG signal (low-amplitude ECG dispersion). Deviances of the electrophysiological properties upon different pathological processes lead to changes in the alteration amplitude. For this reason, such changes precede the changes of ECG itself. For this reason, the low-amplitude vibration characteristics can be used as efficient diagnostical markers of approaching the functional myocardial alteration.

According to the measurement procedures, ECG DM can be referred to the method of recording the ECG microalterations. The above methods provide a relatively new noninvasive way to control the myocardial electric instability, which appeared more than 20 years ago ago as the “MTWA method”. The record and analysis of the microvolt alterations differ in principle from the record and analysis of the ECG waves. The microalterations are calculated as ECG-signal microvibration in the consecutive cardiac beats. The microalteration amplitudes can be less by two orders of magnitude than the standard ECG wave amplitude. The microvolt alterations lose completely the information on the amplitude features of the original ECG waves, *i.e.*, the microvolt alterations appear as a random process, which includes no original properties of the ECG-waves in the derivation under analysis.

The simplest and chronologically first method to register the microalterations includes measuring the difference between the synchronic amplitudes of current and previous ECG waves of the same type; for example, that of T-Wave. Such method of analysis is usually referred to as the “from beat to beat” method. The correlation between ventrical fibrillation probability and the presence of periodical s-signal microvibrations with the main frequency being approximately twofold less than heart rate (HR) was found. If such vibrations would be filtered and their energy spectrum would be estimated, one can detect the increase in the microvibration almplitude. It is just this fact that indicates the increased predisposition of the myocard to the ventricular tachycardia or fibrillation. This method allows one to record the T-Wave microalteration signal only at the HR of ~ 100 beats per minute only. The main difficulty of this method is to achieve the acceptable signal/noise ratio, since the wideband physiological noise increases dramatically with increase in the HR. The essential necessity of the stress-load during several minutes is the second disadvantage of this method. Despite a high sensitivity to the myocardial electrical instability, due to these disadvantages the above method is poorly acceptable for the screening procedures of early detecting the myocard prenosological changes. Now, this method is used in “CH-2000” device of the American firm “Cambridge Heart” preferably for ventrical fibrillation prognoses when cardiac pathology exists.

The other methods of ECG microalteration registration are based on the secondary estimated indications obtained from the original ECG analysis. The point of these methods is the following: some estimated ECG properties have the essentially better signal/noise ratio than the spectral characteristics of above analysis. To estimate the secondary characteristics, the certain mathematical model establishing relation between the ECG being registered and estimated microalterations secondary characteristics shall be used always. In the ECG DM method, the mathematical model for the voltage calculation between closely located interfacial points based on the model account of myocardial electromagnetic emission is used. The physics of this model consists in the unbiased dependence between the average microalteration amplitude and s-signal characterizing the electrical symmetry between the right and left ventriles and between the right and left atria *[31]*, *[45]*.

To calculate the microscopic alterations of electric symmetry, the cardiac electric biogenerator model of high accuracy is necessary. The traditional biophysical models for creating the superficial ECG signal were found to be very rough for such calculations; therefore, the model with more precise account of the electrodynamic effects was used. The analysis of the microscopic alterations of the s-signal electric symmetry gives rise to the ECG microalterations map, which was named as a “dispersion map” in the ECG DM method. The mathematical model proposed allows obtaining the stable ECG microamplitude signal, which reflects not only T-Wave microalterations, but that of the QRS-complex and P-Wave even at rest.

The ECG dispersion mapping method is based on using two groups of factors influencing formation of the superficial cardiopotentials, *i.e.*, the non-linear effects occurring upon activation and deactivation of the contractile cardiac myocyte membrane ion channels; electrodynamic effects occurring upon avalanche processes of the ion current flow through the contractile cardiac myocyte membrane. These factors have not been analyzed within the common linear electrophysiological models describing the cardiac electric biogenerator. The studies performed by the model authors show that account of the above effects allows building the essentially more precise model of the superficial ECG formation and hence widening the diagnostic possibilities of the classic ECG method. Despite using the ECG signal as the sourse of raw digital data, the whole analysis in ECG DM is carried out in the new attribute space generated by the little ECG fluctuations (low-amplitude dispersions). Clinical interpretation of the low-amplitude dispersion fluctuations requires one to understand clearly what is the electrophysiological source of fluctuation signals. This source is represented by two main mechanisms generating the little superficial potential fluctuations, such as molecular mechanisms of the inflow and outflow gates of the cardiomyocyte transmembrane channels and superficial ECG electrodynamic mechanism generation.

***Molecular Mechanisms of the Transmembrane Ion Channels*.**

The biophysical models describing electrical properties of the transmembrane ion channels in the molecular biology and electrophysiology are linear in principle. In common representation, such models describe two main states of the ion channels, such as open-closed, and these states dynamics determined by the linear differential equations. Unfortunately, the linear models do not provide a clear and unambiguous description of the numerous trigger modes (appearing during the different pathologies) for the action potential (AP) formation. In linear models, the kinetics of the trigger mechanisms controlling the jump-type processes of closing/opening the inflow and outflow channel gates in phase 0 and phase 3 of the AP remains out of the analysis. However, namely this kinetics is the most important for the analysis of the AP fluctuation dynamics, which, in turn, influences the superficial ECG fluctuation dynamics.

It may be shown that all the currently known dynamics of the myocard cells is well described with the non-linear model of the potential-dependent ion channel having two unstable points. In this model, mathematical description of the channel wall is equivalent to the description of some elastic three-link hinged arm with two degrees of freedom. The main difference of the non-linear ion channel model from its linear analogs consists in that in its mathematical description, the snowballing process (“catastrophic jumps”) elements emerge, which can not emerge in the linear models in principle. Thus, the channel permeability in the new model acquires the quantized form, and the transmembrane electric potential value and subcutaneous water temperature are the main parameters controlling the transitions between its stable conditions. The transmembrane potential values, at which the ion channel loses its stability, create the instability areas.

In the non-linear model, the ion channel inflow and outflow gates have the “molecular snaps” system. At a certain value of the transmembrane potential U and weak above threshold impulse electromagnetic effect, the channel configuration transfers from one stable condition to another, and the molecular snaps keep its condition till the next above threshold impact. Using the non-linear model, there is no necessity in complicated phenomenology, which normally increases indefinitely when the more precise experimental data are obtained. One of the most important model results is the fact that the intermittent transition from one stable condition to another is accompanied by dramatical enhancement in fluctuation of physical parameters. The AP fluctuations of particular cardiomyocytes generate macrofluctuations of the myocardial de- and repolarization waves in both their space structure and the area of their temporary characteristics. As the myocard is an excitable dissipative medium, one can estimate the AP fluctuations by controlling the fluctuation amplitude of the integral electrophysiological parameters and, thereby, can control the hidden evolution of pathological processes at its early stages. In clinical conditions, due to both simplicity and measuring efficiency , the ECG signal is the most suitable. It is just this idea that forms the technological basis for all control methods of the ECG electric microalteration *[10], [11]*.

Electrodynamic Mechanisms of Superficial ECG Generation.

Despite the above idea seems to be simple, there are many technical difficulties for its implementation. The main difficulty is the following: the ECG microamplitudes being measured within 3…20 μV are comparable to the superficial ECG electrophysiological noise; i.e., it is necessary to apply specific methods of increasing the signal/noise ratio. If one will not do this, the analyzed signals generated by the AP cardiac myocyte fluctuations are erased by the noise fluctuations. The noise fluctuations are caused: first, by the internal thermal noises of an electronic device; second, by the heterogeneous character of the heart-surrounding tissue; and finally, by the multiple muscular tremor effects.

The DM method is chronologically the most recent method of the ECG microfluctuations registration; it includes the algorithm of increasing the signal/noise ratio, which is principally different from its analogs. This algorithm is based on the new model of superficial ECG resulted from the above-mentioned non-linear model of the transmembrane ion channel. This new cardiac biogenerator model takes into account the cardiac myocyte electromagnetic emission at stages 0 and 3 of the action potential.

The most essential descriptive aspects of this model are as follows. Upon AP generation by a particular cardiomyocyte, due to the impulse currents through ion channels, in addition to the common ion currents, which appear within intercellular and intracellular space and follow to Ohm's law, the electromagnetic emission appeared, which corresponds by its spectral quality to the near-infrared radiation with wavelength of ~ 20…90 μm. This emission having high permeability for the pericardiac tissues is absorbed by the skin integument. The epidermis and inner skin create some sort of aerial, which absorbs the electromagnetic emission of cell. The correct account of the myocard electromagnetic emission being disregarded in the traditional models allows eliminating these difficulties to a great degree. In the new model being named by authors as an electrodynamic one, the superficial potential difference is the result of the cardiomyocytes electromagnetic waves interference, but not of summarizing the cardiomyocytes electrostatic fields. Using the DM-technology, some model parameters can be calculated at the ratio error of ~ 3%.

It was shown that the best results according to the criterion of the signal/noise ratio are obtained using the specific lead system. Measuring the s-signals between adjacent derivations in this system during ~ 30 sec using certain algorithm, we can estimate the electric symmetry between the cardiac chambers for each time point of t he PQRST complex; and using the transition formulas, we can calculate the ECG fluctuation amplitudes. For the electrical symmetry signal, the ratio signal/noise is severalfold increased relative to the direct measurement of ECG fluctuation amplitudes. As a result, the stability and frequency of the ECG microamplitude signal obtained by such a method is increased dramatically; and the amplitude can precisely calculated using the extremity lead signals only. To calculate such characteristics, the several consecutive cycles should be synchronized, and the microamplitude registration and secondary model characteristics calculation should be performed in each of them according to the above principles. The final dispersive characteristics have the form of time function.

The dispersive characteristics in a “PARCECG” instrument are calculated over 9 analyzed lead groups (G1-G9), which reflect the degree of manifestation and localization of the electrophysiological disorders in the myocard of atria and ventricles at the de- and repolarization stages. The rank (interval) criteria of the PQRST indication fluctuation changes are represented by the following parameters[1]: ECG-signal dispersion fluctuation areas on depolarization of the right *($DisP_{RV}$)* and left atria *($DisP_{LV}$)*, *i.e.*, (*G1* and *G2*), ECG-signal dispersion fluctuation areas on finishing depolarization of the right and left ventricles (*QRS_{END}–RV)* and *(QRS_{END}–LV*), *i.e.*, (*G3* and *G4*), their repolarization *($DisT_{RV}$)* and *($DisT_{LV}$*), *i.e.*, (*G5* and *G6*), depolarization symmetry index in the middle part of complex QRS (*QRS_{MEAN}–RV-LV*) – G7, intraventricular conduction disorder index– G8, depolarization symmetry index in the initial part of complex QRS (*QRS_{BEG}–RV-LV*) – G9.

In the presence of any pathological changes, the patient respective dispersion line fragments exceed the upper and lower normal limits. The manifestation degree of fluctuations is estimated by the limit excess area. This area, *i.e*., actual manifestation of the fluctuations, shall be estimated by the integral index named as “Myocard” index, or index of the myocard electrophysiological changes (microalternations). The Myocard Microalternations Index (MMI) change within the relative range from 0% to 100%; it is a relative index of deviation value. The microalternations index of 0% corresponds to the full absence of any significant deviations, *i.e*., to position where all dispersive lines are within the normal limits. The more index value, the more deviation from the norm.

In cases where there are no significant deviations from the norm of the recorded mean amplitudes of ECG-signal microvibrations, the integral “Myocard” microalternation index is less than 15% and G1-G9 gradations are near to zero. If the “Myocard” microalternation index has the limit values (15-17%), and G1-G9 gradations have some insignificant fluctuations, it suggests the possibility of some transition process, which can be both the initiation of some pathological changes and consequence of some transient metabolic deviations. Finally, increased values of both the “Myocard” microalternation index and G1-G9 indexes are evidence of significant electrophysiological deviations. The structure of G1-G9 changes allows clinical hypotheses of interpretation of the detected changes for further full diagnostic study.

Some components of the above-described technology of fluctuations analysis during 1996-2005 are patented *[9], [11]*. The medical technology of application of the “PARCECG” device is specified by recommendations *[7], [9], [10], [11], [28], [31], [45]*. The analogous device “CardioDM 06” with some modifications is produced by “Heart View” (USA, Cleveland). When designing the calculation algorithms for “PARCECG”, the initial distinction between the norm and pathology was performed based on the standard training procedure of automatic classifier with the control group of healthy persons, as well as with the group of persons having strictly verified clinic diagnoses including the hypertensive disease, different forms of the ischemic heart disease, cardiac anomaly, *etc*. As a result, for each of the G1…G9 groups, as well as for the integral indexes, the local limits of normal values in ordinal and interval scales were defined.

The “Rhythm” indicator index is calculated based on the Bayevsky algorithm for the PARS index modified by the authors to work at short samplings. In addition to the main two microalternation indexes “Myocard” and “Rhythm”, in the “CardioDM 06” instrument, the additional two-axis indicator of the myocardial electric instability within the *TW-Alternans* – “T-Wave Microamplitude” and *Variational parameter* – “PR-Variation Pared Coefficient” axis is calculated. The Variation Pared Coefficient (WPC) is defined using the formula proposed by R. Bayevsky: $WPC = (SDNN) \cdot 100 / RR_{av}$, where SDNN is the standard deviation of the RR_{av} interval, which is an average value of the interval between the adjacent R-waves in ECG. The above-mentioned indicator allows reliable differentiation of the following three gradations of the electric instability probability: high probability, borderline state, and norm; and gives an important operational information when using the “CardioDM 06” to monitor the myocardial dynamics. In addition to the “MYOCARD” and “Rhythm” integral indexes, the instrument provides automatic table representation of the results of T-wave alternation analysis at three points: t_{start}, $t_{maximum}$, t_{end}.

[1] The original values of dispersion deviation areas is measured in the units [μV×msec]; however, to increase the output characteristics stability, the original values should be converted into ordinal (interval) scale

In the “PARCECG” instrument, the dispersive characteristic chart is projected onto the surface of computer 3-D cardiac anatomy model, the so called “cardiac portrait” or quasi-epicardium. The “cardiac portrait” takes two forms: from the side of right atrium and right ventricle, and from the side of left atrium and left ventricle. These two types do not correspond to the cardiac anatomy position in the thorax. The observation angle in the computer model is selected to provide the best color and spatial division of the dispersion indicators. The “cardiac portrait” in the ventricle area reflects the integral pattern of dispersion changes calculated for both myocardial depolarization and repolarization. The dispersion changes in the “cardiac portrait” in the ventricular region correspond only to the depolarization stage where the pathological and normal areas of the ECG signal dispersions are color-coded. The Gaussian distribution areas of distribution characteristics are colored in green. Upon the different deviations, the color in the area of changes varies from green to yellow or red. The more their area, the more deviation from the norm. The “portrait” color changes upon both deviations of the temperature characteristics and delay or advance of dispersion characteristics correlating with the P-Q, Q-T, QRS interval values.

The method is sensitive, but non-specific with regard to the factors affecting the myocardium and damaging reasons of the microalternation characteristics. The DM-indexes serve first of all as indicators of metabolic disorders due to the changes in coronary microcirculation, microvascular resistance and collateral circulation and, to a less degree, indicate the severity of epicardial arterial occlusion and heterogeneity of regional perfusion, compensatory mechanisms of the myocardial blood flow and their deterioration, which lead to the changes in the myocardial electrophysiological characteristics.

DM Indexes of Healthy Persons

The Dispersion Mapping is a new method used in cardiological clinical practice for earlier detection of the myocardial electrophysiological properties. Currently, thanks to development of the prenosological diagnostics *[16]*, *[19]*, *[52]* aimed at the study of the borderline states between the normal and pathology, the question now arises of whether this method can be used to determine the degree of abnormality. The current health centers posses a high potential to detect the individual risks of cardiovascular diseases *[12]*, *[14]*. This is caused by introducing the innovation diagnostic technique complex, including the analysis of the ECG-signal microalternations, *viz*., Dispersion Mapping *[12]*, *[14]*, *[16]*, *[25]*, *[26]*, *[52]*.

Age Dependence of the DM Indexes

The analysis of dynamic changes in MMI in the population of healthy persons showed the increase in the mean values with age in the following 4 selected ranges: 20-30 (n = 22), 31-40 (n = 23), 41-50 (n = 20), and 51-60 (n = 18), which was 11,8±1,4%, 12,5±1,9%, 13,5±1,1%, and 14,2±1,1, respectively. Also, the reproductibility analysis was performed based on examination results of 83 healthy persons (47 males and 36 females) at the age from 20 to 60 years (average age 38,3±0,6 years) without any anamnestic, physical, electro- and echocardiographic, roentgenologic, and laboratory indications to any heart, lung, and other organ diseases *[31]*, *[45]*. The “Myocard” microalternation index increased in statistically significant manner and was maximum (14,2±1,1%) in the group of 51-60 years. No statistically significant increase in the “Rhythm” index was revealed. However, it should be noted that certain differences can be obtained upon comparison of similar age groups, which differ in the level of physical activity. A statistically significant increase in the G4 and G5 dispersion indexes was found in the age group of 40-60 years (36.3±5.4 and 30.6±7.7 μV×msec, respectively). As it follows from the data obtained, in the group of healthy persons of 40-60 years age, the T-Wave alternation indexes at three points t_{start}, $t_{maximum}$, t_{end} increased in the beginning of T-Wave and at the peak point (6,3±0,5 μV and 9,2±0,5 μV, respectively) and trend to increase was noted in the T_{end} (8,1±0,5 μV) point. In the age group of 20-40 years, such indexes were 3,3±0,4 μV; 6,7±0,4 μV, and 6,6±0,5 μV, respectively. The presence of age differences was evidenced by the data of V.V. Pronina, S.I. Fedorova, and T.Y. Lebedeva, who studied 70 healthy persons at the age from

20 to 56 years in the age groups of 19-25, 26-35, 36-45, and 45-56 years. In the selected groups, the MMI values were 11,5±4,4%, 14,1±2,3%, 14,9%±0,5%, 14,6±3,2%, respectively *[85]*.

Nearest and Remote Reproducibility of Results.

The data on the nearest and remote reproducibility of the DM indexes are poor. The data of A.A. Katyrev *et al*. *[64]*, *[65]* in examination of 261 patients allowed conclusion of a high reproducibility of the method and results obtained upon determination in different hours of the same day, different days of the same week, in week, in 1 and 6 months. According to our data, no significant differences between the digital data of three consequent measurements were found *[31]*, *[45]*, which suggests a good nearest reproducibility of results. The MMI value in the first measurement in men is slightly higher (14,4±1,2%) compared to that in women (11,2±0,9%) upon the first and following measurements. In addition, note that in 10 cases (12%) among 83 healthy persons under examination, the MMI value was more than 15% in the first or second of three successive measurements. For 5 persons (5%), the values of this index exceed the normal value in all three consequent registrations. The nearest and remote reproducibility of results according to the characteristics of automated conclusion and the alternation amplitude indexes estimated separately is quite high. This concerned firstly the G3, G4, G5, G6, and G8 indexes where number of coincidences was from 62 to 87%.

Indications and Fields of Application

Dispersion Mapping can be applied routinely in any field of medicine that requires diagnostics and early detection of changes and abnormalities in the myocardial electrophysiological properties. It can be used as both independent technique and additional method to estimate the myocardial condition in combination with the standard electrocardiography method.

The current data on application of DM in clinical practice showed that this method can be used efficiently upon screening and preventive medical examination of any group of population *[12]*, *[14]*, *[26]*, *[27]*, *[65]*, *[99]*. So, according to S.Y. Glova *et al*. *[28]*, *[29]*, upon screening of 1350 persons, the diagnostic efficiency of the instrument was 75%. The method is recommended for supervision of healthy persons *[16]*, *[17]*, *[18]*, *[19]*, *[35]*, *[62]*, *[114]* in sports medicine *[70]*, *[111]* and aeroastromedicine *[20]*, *[22]*, *[37]*, *[72]*, *[79]*.

The interesting data were obtained when using the DM method for monitoring the therapeutic effectiveness in different groups of patients: upon the infusion therapy with Reosorbilact in patients having the out-of-hospital pneumonia *[75]*, treatment of the arterial hypertension *[71]*, *[76]*, chronic cardiac insufficiency *[80]*, ischemic heart disease *[4]*, *[77]*, *[78]*, *[89]*, *[92]*, *[94]*, and depression *[21]*, dynamic observation and monitoring of the myocardial condition in patients with different disease affecting the myocardium *[6]*, *[7]*, *[8]*, *[41]*, upon rehabilitation *[39]*, *[40]*, *[48]*, *[116]*, effects of different external factors on human *[30]*.

Of considerable interest are preliminary data on DM application in persons having professional stresses: railway employees, personnel of the EMERCOM, air staff, *etc*. *[17]*, *[18]*, *[62]*, *[79]*, *[99]*, *[103]*, *[105]*, *[112]*, *[113]*, *[115]*. The detected changes in the DM indexes allow the authors to recommend the method for prenosological control, which was confirmed by a series of other studies. Upon examination of 1200 pupils and 330 air company employees, R.M. Bayevsky *et al*. revealed the significance of the method for prenosological diagnostics of children and adults *[16]*, *[19]*. It was shown that in such cases, estimation of the organism adaptative capabilities requires deep understanding of the interaction processes of different parts of the adaptation mechanisms. The adaptive reactions of the cardiovascular system depend also to a considerable extent on the myocardial electrophysiological properties and its ability to response adequately on different loadings. In the works of G.V. Ryabykina and N.A. Vishnyakova (2008-2009), no gross sensitivity errors were revealed upon examination of 1000 persons at the age from 20 to 80 years, the instrument indicated in the majority of cases the significant deviations, which were confirmed by the verified diagnosis *[24]*, *[25]*, *[89]*, *[90]*, *[91]*, *[102]*.

It was established the long-term prognosis of the acute myocardial infarction depends on the IHD duration up to hospitalization [38], [42], [40], [47]. S.I. Fedorova, V.P. Pronina *et al.* performed a series of patient examinations to detect any changes and disorder dynamics of the myocardial de- and repolarization properties upon different endocrine pathologies [3], [82], [96], [109]. For the moderately severe diabetes mellitus of 2 type and severe course of the disease, the direct correlation of the MMI with the triglyceride level and atherogenic index was established [3], [106], [107]. It was noted that the changes in the MMI take place with decrease in the glucose concentration and during the increasing hyperglycemia [95]. It was shown that the use of MMI monitoring is efficient to estimate the myocardial damage upon plasmapheresis [69], photoautohemotherapy upon alcohol intoxication in the CKD patients undergoing the peritoneal dialysis [83], [84], [104]. The early preclinical manifestations of cardiac pathology were detected upon application of "PARCECG" in the patients with the joint hypermobility syndrome [36] and ones having the pectus excavatum [55], [86] upon estimation of the defibrillating effect.

The presence of the cardiostimulator, continuous ciliary arrhythmia, or auricular flutter, paroxysmal event of the supraventricular or ventricular tachycardia, age less than 14 years, and bundle branch block restrict application of this method. The pharmaceutical compositions can influence the ECG-signal microamplitude indices under analysis, *i.e.*, when analyzing the dispersion deviations under the massive medicamental impacts on the myocardium and coronary blood flow, these factors must be taken into account. When using the instrument for treatment, the comparison of the current values and results obtained prior to or at the beginning of drug therapy is obligatory.

Diagnostic Consideration

There are many studies performed to analyze the diagnostic consideration of DM in estimation of the cardiovascular system upon medical examination and screening. For example, according to A.S. Sula, G.V. Ryabykina, and V.G. Grishin, on examination of 213 patients, the average sensitivity and specificity indices of DM to ischemia were 79% and 76% [100], [102]. According to P.V. Struchkov [99], on examination of 700 patients, the sensitivity of this methodology was 76% and the specificity was 64%. According to S. Tsek *et al.*, on examination of 335 patients at the age from 40 to 70 years, the sensitivity and specificity values of DM were 95% and 92% for detecting the myocardial ischemia, 75% and 74% for detecting of the left ventricle hypertrophy, 60% and 75% for detecting of the myocardial electric instability [112], [113]. When using DM for detecting of the HID, N.A. Vishnyakova established the sensitivity of 93% and specificity of 75% [24], [25]. According to S.Y. Glova *et al.* [29], upon screening examination of 1350 inhabitants of Rostov-on-Don, the average values of sensitivity and specificity were 83.3% and 66.6%. The similar results were obtained in other studies [23], [34], [35], [61], [64], [66], [67], [103], [112], [116]. The results of the DM application showed that the method helps to detect the group of persons with the statistically significant changes in the cardiovascular system during medical examinations and allows one to supplement significantly the traditional ECG examination. For example, the data of A.A. Katyreva *et al.* [64] obtained upon examination of 359 patients confirmed that DM is an informative medical test.

Functional Tests

There are too many fields of possible applications of DM, including mainly the fields of medicine and applied physiology where the question is a division of the prenosological and premorbid states in the area of transition from the norm to pathology or from pathology to the norm. Especially, it relates to estimation and prognosis of the functional status of persons being subject to the continuous stress impacts. Therefore, some special studies are necessary to detect the diagnosis and prognosis significance of DM for healthy persons during various stress impacts of the industrial, social, emotional, and environmental nature.

It is reasonable to use the functional tests and take into accout the frequency-dependent changes in the DM indexes. The analysis of DM indices during the test can be a useful instrument, which increases the informational content of the test. The functional tests are an important part of Dispersion mapping and provide essential additional information for estimation of the cardiac functional state. They allow estimating both the original data deviation and, according to their dynamics, the characteristics of compensatory reactions and regulatory systems. Besides the analysis of the responsiveness of vegetative systems and vegetative provision of activity, it allows revealing the changes in the myocardial electrophysiological characteristics changes due to the changes in blood supply and metabolism, and other constituents of the multilevel and complex organization with non-linear multilateral direct and inverse relationships.

The adaptive reactions of the cardiovascular system depends mainly on both the myocardial condition and its ability to response adequately to different loadings. In this context, the DM analysis of the myocardial electrophysiological characteristics is important and promising. Estimation of these diagnostic tests can be regarded as a novel methodological approach for early detection of the above-mentioned disorders, development of the indications for further dynamic monitoring and controlling the therapeutical efficiency.

Influence of Psychological Stress on the DM Indices

Various stressors, including psychologic stress, can affect the myocardial electrical stability up to progress of the potentially dangerous and ominous arrhythmia *[18]*, *[52]*, *[60]*, *[62]*, *[81]*, *[114]*. In this section, the results from examination, which we performed on 25 conditionally healthy persons at the age from 25 to 55 years, are presented. The 2nd group included 20 healthy persons (16 male and 4 female) being employees of the intensive care unit at the age from 24 to 58 years. Examination of employees was performed as follows: the stage I – before their duty, stage II – 1 day after the duty. The persons having any cardiac diseases were excluded. The mean values of calculated variance parameter (G1-G6), depolarization symmetries (G7), intraventricular blocks (G8), and ventricular hypertrophies (G9) (μV×msec) were analyzed *[31]*, *[45]*. When analyzing the dispersion indices from G1 to G9, the significant difference between the indices of healthy persons and employees of the intensive care units were found according to a series of indices. At the stage II, in a group having the stress, the significant increasing more than 2 times of the RV depolarization index (G3 - 70,5±14,3) and that of the LV (G4 - 73,6±12,7) comes under notice. In addition, the parameters G5 increased (from *16,1±3,0 μV×msec* to *25,4±3,7 μV×msec*, respectively).

Test with Isometric Contraction.

The analysis of ECG dispersion mapping indexes obtained upon the tensor test in 37 healthy persons at the age of 34±11 years showed a trend to increase in the myocardial microalternations index and G5+G6, as well as significant increase in the G3 index (from *36.9±15.4 μV×msec* to *89.5±19.6 μV×msec*) *[60]*. When performing the tensor test in patients having the cardiovascular pathology, examination included the data for 5 groups of patients (n = 76) as follows: the 1st – with the arterial hypertension (n=16), 2nd – with the ciliary arrhythmia paroxysmal events (n = 20), 3rd – with the postinfarction cardiosclerosis and ventricular arrhythmia (n = 13), 4th – with the postinfarction cardiosclerosis without arrhythmia, 5th – with the postinfarction cardiosclerosis with the CI of II-IIIFC (n = 14), 6th – with the alcoholic cardiomyopathy (n = 13). The results of 114 samples from 37 conditionally healthy persons were analyzed (the average age is 44.5±8.6 years). According to the data obtained, the MMI indexes were maximum in groups 3, 4, and 5 (21.3±0.9%, 29.6±0.6%, 26.7±1.8%). During the tensor test, the highest increase in the index was detected in the group having the paroxysmal event MA (to 32.5±1.2%); while there were no significant changes in groups 3 and 4. Note that the Myocard microalternation index decreased in group 5 (from 26.7±1.8% to 17.9±1.9%) both at the peak of test and after its completion. The maximum increase in the analyzed G1 and G2 indexes before loading was detected in the 3rd group (postinfarction cardiosclerosis with ventricular arrhythmia). Upon the functional test, the maximum increase in G1-G2 was noted in groups having the paroxysmal ciliary arrhythmia and postinfarction cardiosclerosis with and without arrhythmia (G1 – *90±9 μV×msec*, *88±11 μV×msec*, *115±29 μV×msec* and G2 – *55±10 μV×msec*, *66±9 μV×msec*, *128±31 μV×msec*, respectively). In groups 5 and 6, the G1 index changed insignificantly. The most pronounced increase in the G2 index during the tensor test was detected in the 4th group. Increase in the microalternation indexes upon depolarization was detected in the 2nd group (postinfarction cardiosclerosis with ventricular arrhythmia) both in outcome (G7 – *63±5 μV×msec* and G9 – *43±5 μV×msec*) and during the functional test (G4 – from *233±25 μV×msec* to *281±21 μV×msec*). After completion of the loading, the indexes in the group with the paroxysmal ciliary arrhythmia returned to their original values. At the 2-3rd minute after loading, the maximum increase in the G7 index remained in the 2nd group.

Prior to loading, the maximum increase in the G5 and G6 indexes was detected in the 3rd group (*116±32 μV×msec* and *102±48 μV×msec*, respectively). During the functional test, the maximum increase in G5-G6 was detected in the healthy group and was more than fourfold higher compared to the outcome (*129±27 μV×msec* and *94±28 μV×msec*, respectively). In the 4th group, the increase in the G6 index was detected; and in the group with paroxysmal ciliary arrhythmia, only the trend to increase on loading remained. The G5 index of patients with the cardiomyopathy of alcoholic genesis decreased significantly from *108±22* to *54±24 μV×msec*.

T-Wave Alternation Data in Three Points (t_{start}, $t_{maximum}$, t_{end}) in the groups under examination at the step of tensor test showed their significant increase in all groups prior to test *[38]*, *[43]*, *[54]*, *[58]*, *[59]*, *[98]*. A high T-Wave alternation reaction was detected in all three points: t_{start}, $t_{maximum}$, t_{end} (respectively, *19.7±1.3 μV*, *26.4±0.7 μV*, and *18.4±1.9 μV*) in the group with the MA paroxysmal events, whose values returned rapidly to the original ones after completion of loading. In the groups with the postinfarction cardiosclerosis, the reaction of the $t_{maximum}$, t_{end} indexes upon this test was weakly pronounced (at high original values), and the t_{start} values decreased. In the 2nd group, at the 2-3rd minute after loading test, the significant increase in the t_{start} and t_{end} indexes was detected.

Taking into account the data obtained one can assume that the type of response to activation of the sympathoadrenal system activation and beta-receptors condition plays a big role in the genesis of dynamics of the myocardial microalternation index. It is seen from the MMI increase reaction in patients with the paroxysmal ciliary arrhythmia and from decrease in the response in the group with the postinfarction and alcoholic genesis of chronic heart failure, which can suggest the abnormality in the sympathetic provision and reflect the main features of disorder of the myocardial electrophysiological state at different time intervals of depolarization.

The results of another study indicated 3 different types of reaction to physical activity (20 squattings) according to DM performed in 65 patients: 1st – increase in the MMI by 2% and more, 2nd – no reaction, and 3rd – decrease by 2% and more (at high original values) *[39]*. According to E.N. Dudnik *et al*. *[34]*, the average values of sensitivity and specificity upon physical activity were 63% and 100%. When monitoring 188 patients with the IHD and 68 healthy persons during and after the loading tests, V.A. Semyonov *et al*. showed the DM method is valuable not only as screening method, but also as a highly sensitive diagnostic method *[97]*. The similar data on increase in the DM effectiveness using the tests with physical activity were given in other studies *[46]*, *[87]*, *[97]*, *[104]*.

Test with Oxygene Inhalation.

A series of studies was performed in the group of healthy healthy persons and IHD patients (instable angina and acute myocardial infarction) using the test with oxygen inhalation (5 minutes of inhalation with 40% content of resuscitation oxygen). The analysis of changes in the MMI showed its increase at the 5th minute in both the control group and group with the instable angina and myocardial infarction ($p < 0.02$); although no reaction was observed in some cases. For example, the MMI increased from the initial value of 14.4±1.3% to 20.6±1.6% at the 5th minute in the control group, from 21.7±1.9 to 28.3±2.4% in the IA group, and from 26.2±1.8% to 33.7±2.0% in the MI group *[45]*.

In the group with the MI, the stable and significant increase in the areas of the *P (G1+G2)* wave dispersion deviations was observed at the 3-5th minute of inhalation, while this values fluctuated in the group with IA, namely, increased at the 1st minute and decreased at the 3rd minute. The *P* wave dispersion deviation amplitude indexes in the IA group decreased significantly to the 3rd minute ($28.1\pm3.1\ \mu V\times msec$). In the IA and MI groups, the areas of dispersion deviations of the *QRS (G3+G4)* complex remained unchanged and the *T (G5+G6)* wave indexes decreased significantly 1 minute after inhalation, but returned to their original values at the 5th minute. In total, the mean amplitudes of dispersion deviations *(G1-G6)* in the patient groups under examination repeated the dynamics of deviation areas. Discontinuity of the changes in the DM index in the P wave, QRS complex, and T wave was detected in the IA and MI groups upon testing with oxygen inhalation. This can be due to the heterogeneity of pathophysiological processes and postishemic disfunction in different regions of the myocardium. Different variants of microcirculatory and perfusion changes can occur upon oxygen inhalation depending on the recrudescence terms and severity of vascular damages.

DM Indexes in Healthy Persons upon Treadmill Test According to the Data of CH-2000 and PARCECG instruments

One of the new methods increasingly used in the scientific researches and routine clinical practice is the T wave alternation analysis (TWA). The operating principle of a CH-2000 instrument (Cambridge Heart, USA) is based on the analysis of the T-wave low-amplitude vibrations of the ECG signal upon graduated physical load and can be used to detect the ominous arrhythmia risk groups. The results obtained during testing the CH-2000 of "Cambridge Heart" and "PARCECG" systems upon synchronous registration using two instruments were compared *[45]*, *[58]*. In the initial state prior to exercising, two consecutive examinations in prone position on a PARCECG (HV1 and HV2) instrument and one ECG HR record were performed. Then, the exercise test was performed and ECG was recorded on a CH instrument according to the "Cambridge Heart" recommendations: the 1st stage – 2.5 minutes with retention of the heartbeat rate in the range of 100-110 beats per minute (T1), and the 2nd stage – 1.5 minutes with retention of the heartbeat rate in the range of 110-120 beats per minute. When any contraindications to testing appeared, the test was terminated. On reverse passing through the heartbeat rate of ~ 100 beats per minute (decrease in the physical activity), two consecutive examinations, *viz*., HV3 and HV4, were performed. The first examination with recording the ECG on a PARCECG instrument after exercising (HV3) was performed at the HR of 100…95 beats per minute. 4-5 minutes after stopping the track, two consecutive examinations (HV5 and HV6) were performed. After completion, DM was rerecorded for 5 min. To analyze the T wave alternation along with simultaneous use of a PARCECG instrument, the heartbeat rate run was performed according to the standard operational "Cambridge Heart" recommendations. During the exercise test in healthy group, the T wave alternation indexes were estimated at three points: t_{start}, $t_{maximum}$, t_{end}.

The group of 71 healthy persons was examined; they were examined using the above-mentioned techniques for the treadmill test (29 persons at the age from 20 to 40 years and 42 persons at the age from 40 to 70 years). Among 105 tests in healthy persons, the automated CH diagnostics showed the presence of the "stable T wave alternation and signs of positive test" in 4 cases (4%) (among them, the nodal extrasystole was in 2 cases, atrial extrasystole was in 1 case, and 1 person was almost healthy). An ambiguous result with recommendation to repeat the test was in 24 cases. The comparison of the data obtained on two instruments showed good agreement of the average T wave alternation values at the second (CH-2000 – *12,3±0,5* and *8,1±0,8 μV*) and third steps of monitoring (CH-2000 – *11,4±0,6* and *9,0±0,8μV*). It is important to note that the dynamics of MMI amplitudes showed 3 amplitude variants upon consecutive monitoring during rehabilitation for 5 min. In the majority of cases (75%), the fluctuations in the absolute values of myocardial microalternation indices were within 7-9% and did not exceed the upper range of average values of 15% in healthy persons. In 22% of cases, the fluctuations from measurement to measurement (after 30 sec) were higher, *viz*., from 10% to 17%. And in 2 cases (3%), the fluctuations of the MMI absolute value were more than 20%.

The analysis of the dynamic results of the MMI changes in the control group showed that the original index values in the age group from 20 to 40 years were lower and no significant increase in the nearest rehabilitation period was revealed in this group. In the age group of 40-70 years, the increase in the index up to 17.0±0.4% was noted immediately after exercising, its sufficiently high values remained at the 4-5th minute, and higher heartbeat rate values were noted after completion of the exercise test. The T wave alternation indexes were higher significantly in the age group of 40-70 years in the T wave points 2 and 3 during the first 30 sec of exercising (*12.5±0.4 μV* and *11.3±0.4 μV,* respectively). In the group of 20-40 years, no significant increase in alternation was revealed in all three points (T_{start}, T_{max}, and T_{end}), while in the elder age group, the increase was significant and remained at the 4-5th min after exercising.

Estimation of the Coenzyme Q10 Effect When Using DM upon the Treadmill Test

Of special interest is the study of DM capabilities for estimation of fine changes in the myocardial electrophysiological properties under the action of medicaments decreasing adverse electrophysiological changes during stresses and physical activity *[31]*, *[45]*. The study included the examination data of 37 conditionally healthy persons without any anamnestic and ECG signs of cardiac diseases (the average age is 47,3±4,8 years). Examination with functional test was performed in 3 steps: the 1st – in the outcome, 2nd – after monthly course using the coenzyme Q10 at the dose of 120 mg per day, and 3rd – 2 months later. The control group consisted of 47 healthy persons receiving no coenzyme Q10, which underwent examination using the above techniques and treadmill test (29 persons at the age of 20 – 40 years and 18 persons at the age of 40 – 70 years).

The detected significant decrease in the MMI from 15.4±0.4% to 13.6±0.5% ($p < 0.02$) at the 2nd stage prior to the exercise test should be noted. At the 1st stage, the reaction to exercising was characterized by increase in the “Myocard” microalternation index immediately after exercising (17.1±0.4%); the same profile of changes remained at the 2nd and 3rd stages after the coenzyme Q10 course. The average values of the “Myocard” microalternation index were the lowest at the 2nd stage. The MMI values and its average values upon the treadmill test changed during the two-month course with the coenzyme Q10.

The coenzyme Q10 intake caused decrease in the depolarization indexes (G5 and G6) at the 2-3rd stages upon the exercise test and exceeded moderately the original data (before exercising). A considerable increase in the depolarization indexes (G3-G4) was observed upon physical activity and remained at the 4-5th min after the treadmill test. However, there were significant increase in the G1 and G2 indexes after the two-month course (stage 3) and decrease in response to to the testing loading of the G1 data. The mode of (approximately twofold) increase in the G2 index at the 1st minute after exercising, which was noted at the 1st stage, did not change. In addition, the increase in deviation of the dispersion characteristics in the middle terminal part of the QRS complex (G8 index) was detected. One should also note significant increase in the T wave alternation index in the T_{max} point up to *10.0±0.7 μV* at the 3rd stage in the outcome during the coenzyme therapy and up to *14.0±0.8 μV* ($p < 0.02$) after the exercise test.

Diagnostic Criteria of the Transient Myocardial Ischemia According to Dispersion Mapping upon the Treadmill Test in the IHD Patients.

This work is aimed at the complex analysis of the ECG-12 indexes and ECG dispersion mapping upon the exercise test in the group of IHD patients *[48]*, *[49]*. It was shown that there are two main variants of changes in the test results: with normal and abnormal timed metabolic adaptation. The values of $HR_{max}/MMI_{max}<3.5$, $\Delta HR_{max-min}/\Delta MMI_{max-vin}<2.0$ (frequency-metabolic adaptation index), and myocardial microalternation index > 30% at the heartbeat rate peak characterize a group of patients with the myocardial ischemia and abnormal metabolic adaptation during the treadmill test in the IHD patients.

The study involved 143 patients, who were in the City Clinical Hospital 53 from October 2010 to December 2011 with the diagnosis of IHD I-III FC stenocardia according to the Canadian Classification; they include 99 males and 44 females at the age from 39 to 60 (on average 50.6 ± 4.6 years). In the present work, the test data obtained were divided into 4 groups:

- *1st group* included 47 persons (33%) with negative test results corresponding to the following values: $HR_{max}/MMI_{max} > 3.5$ *and* $\Delta HR_{max\text{-}min}/\Delta MMI_{max\text{-}min} > 2.0$,
- *2nd group* included 60 patients (42%) with indexes: $HR_{max}/MMI_{max} < 3.5$; $\Delta HR_{max\text{-}min}/\Delta MMI_{max\text{-}min} < 2.0$ (positive test result),
- *3rd group* included 21 patients (15%), who within nearest 3-4 were subject to the coronary angiography (CA),
- *4th group* included 15 patients (10%) having the asynchronous dynamic reaction of HR and microalternation indexes during physical activity.

In the above-given data on the diagnostic consideration of DM, we used as a criterion of positive response (the presence of IHD) upon the stress test the following threshold levels for: $HR\ index_{max}/MMI_{max} < 3.5$; $\Delta HR\ index/\Delta MMI < 2.0$, and *the MMI index >30%*. The sensitivity of these indices for the detection of IHD was 78% and the test specificity was75% *[48], [49]*.

Thus, the increase in the DM indexes compared to the control group was noted at the highest load in the both groups of IHD patients; however, the degree of manifestation of this reaction had significant differences. In addition, upon the normal reaction in healthy persons, the DM values returned to the normal rate at the 1-2 min of the rehabilitation period; while the recovery time in the IHD patients with positive test increased.

It is important to note that non-coincidence of the maximum values of heartbeat rate and MMI (asynchronous reaction) took place in 15% cases and their differences were up to 1.0-1.5 minutes; *i.e.*, the highest values were recorded not at the peaking load, but before or after its peak. No significant depression of the ST segment was observed. Upon division of the groups of healthy persons under examination (n=37) and IHD patients (n=107) according to the index of $HR_{max} / MMI_{max} < 3.5$ at the peak of loading, sensitivity of the treadmill test for detection of the IHD was 91% and specificity was 67%. Addition of the changes obtained according to echocardiography to the ST depression index as an index of the myocardium structural damage, the DM sensitivity for recognition of the "myocardial pathology" was 92% and the specificity was 78%.

DM Indexes in Patients with Arterial Hypertension

According to our studies, the analysis of DM indices in the patients suffered from arterial hypertension allows early detection of abnormalities in the myocardium electrophysiological properties *[50], [57], [68], [71]*. Significance of the changes detected consists in that they should be considered as damage markers of target organ upon arterial hypertension (AH) along with other myocardial changes (*e.g.*, echocardiography indexes). Consequently, it appears that the DM data can be used for stratification of cardiovascular adverse event risk upon AH.

The average integral indexes "Myocard" and "Rhythm" for this group of patients were 18.2±0.96% and 43.5±7.3%, respectively, which higher significantly than those in the control group ("Myocard" was 12.9±0.6% and "Rhythm" was 24.3±1.8%). As it follows from the data obtained, the areas of dispersion deviation in patients with the LV myocardial hypertrophy upon depolarization of the left ventricle (G4) were not greater than those for the control group ($16.0\pm2.7\ \mu V\times msec$ and $15.8\pm1.9\ \mu V\times msec$, respectively), but were greater significantly upon depolarization of the RV (G3 – $76.0\pm9.2\ \mu V\times msec$) and LV (G6). The dispersion deviations of ventricular depolarization dispersion were at most twofold greater than those for the control group; while the dispersion deviations of RV depolarization increased to a greater degree. One can assume that the increase in G3 reflects the compensatory reaction of right heart and that of G4 reflects abnormality in the diastolic properties of the left ventricle.

The study on estimation of the diagnostic capabilities of magnetocardiography and dispersion mapping for detecting the left ventricular hypertrophy and for electrophysiological remodeling in the patients with arterial hypertension. The study involved 162 persons. It was shown that magnetocardiography and dispersion mapping can be used for diagnostics of the left ventricular hypertrophy and abnormalities in the myocardium electrophysiological properties and its electric heterogeneity. When comparing the diagnostic characteristics of the left ventricular hypertrophy for magnetocardiography and ECG-12 repolarization indexes, one can conclude that the supposed criteria predominate the known criteria for the standard ECG. In the order of decreasing the sensitivity and specificity, these methods are arranged in the following order: MCG, DM, echocardiography, and ECG-12 *[50]*. According to S.E. Mostovoy *et al*., the DM indices in the AH patients correlated with the flow rate from the left ventricle *[75]*.

ECG Dispersion Mapping in Estimation of Abnormalities in the Myocardium Electrophysiological Properties in Patients with Paroxysmal Ciliary Arrhythmia against the Background of IHD

Diagnostic and predictive capabilities of the ECG dispersion mapping for noninvasive estimation of abnormalities in the myocardium electrophysiological properties in the IHD patient with the paroxysmal ciliary arrhythmia were studied *[5]*, *[38]*, *[59]*, *[98]*. The study included 184 persons; among them, there were 90 patients with different clinical courses of the ciliary arrhythmia against the background of the IHD. The control group consisted of 94 conditionally healthy persons. As the study showed, significant differences of the ECG dispersion mapping indices were detected in patients with different variants of clinical course, nearest and remote outcomes of the paroxysmal ciliary arrhythmia. Significant changes in the ECG-HR indices and heart rate variability were revealed in the patients with different variants of the clinical course of ciliary arrhythmia. The prognostic value of the threshold level of the “Myocard” integral index and the total index of the G1+G2 atrial depolarization microalternations to predict the remote outcome in patients with the paroxysmal ciliary arrhythmia was established, namely, the MMI value more than 20% and G1+G2 more than $40\ \mu V \times msec$ are threshold criteria to estimate the possibilities of development of the MA occasional paroxysmal events in patients with the paroxysmal ciliary arrhythmia against the background of the IHD in the case of unfavorable remote outcome.

Oxidative Stability of Plasma and Blood Lipids Indexes in Patients with Different Forms of IHD

The relationship between the oxidative stability of plasma, blood lipids indexes and severity degree of quinsy was studied in 253 patients with the stable effort angina II FC (n = 130) and III FC (n = 123) *[13]*, *[45]*. The analogous indices were studied in 16 patients with ACS (instable angina), 30 patients with the myocardial infraction in the medical history, without angina, and 40 healthy persons. The MDA level in the IHD patients increased gradually with increase in the severity of angina. In the patients having the MI without angina in the medical history, the MDA concentration was significantly higher by 15% than that in healthy persons. Patients with the angina II FC had the MDA concentration, which exceeded this index value of patients with the myocardial infraction in the past medical history, without angina by 28% and 46% was higher than the healthy group index. Patients with the instable angina showed the maximum degree of their plasma oxidation characteristics – the difference compared to the III FC patients group was 25%. The close relation between the MDA level/ml of plasma and FC angina ($r = 0{,}63$, constraint force $r^2 = 0{,}36$, $p < 0{,}01$) was detected.

Dynamics of the DM indexes and free-radical plasma oxidation between patients with the acute coronary syndrome, as well as their dependence on the disease course and remote outcome were studied. The data analysis of 96 patients with the acute coronary syndrome (ACS) was performed in Day 1, 5-7 of disease (the average age is 64,5±3,6 years). The 1st group included 23 patients with the

MI of Q-type development, the 2nd group included 28 patients with output being not in the *Q*-type of MI, and the 3rd group included 45 patients, whose dynamics of observation showed no signs of AMI. The results for 65 persons were monitored. Among them, during a year there were 14 fatal cases, 17 cases of rehospitalizations, and 34 cases without hospitalization. The analysis of the MDA indices at the stages of research depending on the IHD recrudescence before hospitalization (less than 1 day, and more than 1 day) and the disease remote outcome showed that the fatality rate was twofold higher in the group with short recrudescence period before hospitalization; the maximum MDA indexes (101.2±5.9 nmol/ml) were detected; they decreased in Day 5. The maximum diagnostic consideration, as well as maximum sensitivity and specificity indexes relative to the unfavorable remote result were detected in the group of patients with the IHD short recrudescence period before hospitalization (less than 1 day) with the MDA value > 100 nmol/ml of plasma in both Day 1 and Day 5-7 of the disease. It was shown that in the group of deceased persons, the MMI values were maximum within the outcome (24.7±1.9%) and decreased significantly in Day 5 of observation (18,5±2,3%). In the group of survived persons, the index values remained increased persistently also in Day 5 (22.0±2.9%).

According to the authors, the results of study performed allow considering a group of the IHD patients with high oxidation of blood plasma (MDA more than 100 nmol/ml) as a group with more severe course and elevated risk of different adverse events. The plasma oxidative stability disorders are associated with the different IHD forms course severity, and degree of manifestation of the myocardial electrophysiology remodeling as well. The plasma oxidative stability index (MDA>100 nmol/ml of plasma after 24 hours of incubation with ions of Cu) can be used to estimate the IHD severity with high risk of adverse events. Worsening the ECG HR indexes reflects severity of the IHD course and changes in the same direction with the plasma oxidation index. The QRS complex and P wave indexes amplitude and temporal characteristics can be used for dynamic estimation of the IHD progress, detecting the myocardial ischemia along with the standard electrocardiography methods.

DM Indexes in Patients with Myocardial Infraction

There are great possibilities of increasing the diagnostics of the myocard severity index and electrophysiology properties disorders in patients with the different IHD forms. It is very important to study the dispersion mapping possibilities in the light of existing notions concerning the new ischemic syndromes, taking into account that MD indexes reflect the electrophysiology alternation of cells and their membranes, and associate with the remodeling after the ischemia episode or old myocardial infarction reflect the "electromechanical disharmony" in the myocardial disfunction areas that is very important for researching the arrhythmogenesis. In the studies performed, diagnostic possibilities of DM have already shown a prospectivity of this method for the diagnostics of IHD *[4]*, *[0]*, *[41]*, *[90]*, *[92]*, *[93]*, *[105]*, *[108]* and estimation of different aspects of the AMI course and therapy *[2]*, *[32]*, *[33]*, *[43]*, *[54]*, *[94]*, *[110]*.

DM Indexes Depending on Localizaion of the Acute MI

In a series of studies, relation between the DM indexes and AMI localization was studied. Upon investigation of these groups, the following average MMI values were obtained: the posterior wall AMI (n = 23), MMI- 22.3±2.2%, AMI (20-25c); posterior wall (n = 23) MMI – 21.7±3.3%; anterior wall AMI (n = 25) , MMI – 28.2±3.2%. One can note that significant increase in the threshold value of the "Myocard" microalternation index was only detected in the group with the anterior wall AMI in Day 1 of disease. The increase in the average values of "Myocard" microalternation index in patients with the myocardial infarction was on average 10-15% compared to the healthy persons. The analysis of diagnostic consideration of this index detected high sensitivity values (87.0-83.3%) for the MI different stages and localizations, which coincide with the data of other researchers. The low values of specificity forecasting the value of positive result are demonstrative *[31]*, *[45]*. The following formed parameters have been analyzed: – the ECG-signal dispersion deviation area *totals* values on depolarization of the right and left atrium ($DisP_{RV}+DisP_{LV}$), i.e., (G1+G2) ECG-signal dispersion deviation area *totals* values on completing the the right and left atrium depolarization (*QRS_{END}–RV+QRS_{END}LV*) and their repolarization *($DisT_{RV}$+$DisT_{LV}$*), i.e., (G3+G4) and (G5+G6); maximum amplitude *totals* values of positive (+) and negative (-) dispersion indexes («*peak-to-peak*») of de- and repolarization of the right and left ventricles; average totals values of the dispersion deviations for the *QRS* complex *(QRS_{END}–RV + QRS_{END}LV*), as well as that of the ventricular myocardial repolarization – of the *T wave ($DisT_{RV}$ + $DisT_{LV}$).* The data obtained showed that the patients with the IA and MI demonstrate some differences on the average areas and dispersion deviations amplitudes of the P wave, *QRS* complex, and *T* wave. The detected increase degree correlated with the disease following course severity—with outcome to the stable angina, not *Q*-type of MI and *Q*-type of MI. In Day 5-7 of disease, in the first two groups the *QRS* and *T* indexes, as well as *P* wave dispersion deviation areas decreased. In the group with the *Q*-type of MI, the changes dynamics in the *QRS* complex and *T* wave had the opposite character: in Day 5-7, the (G3+G4) average dispersion deviation values increased, and that of (G5+G6) decreased.

Characteristics of Dispersion Mapping Indices upon Testing by "THE PTB DIAGNOSTIC ECG DATABASE"

In order to analyze the diagnostic capabilities of dispersion mapping, the results of application of the ECG-data reference software, *viz*., the ECG Physikalisch-Technische Bundesanstalt (PTB), *[63]* were tested. The database was collected, annotated, and published by the German National Metrology Institute at www.PhysioNet.org. It includes the data of 549 records performed in 290 persons (at age from 17 to 87 years) with the number of records for each person from 1 to 5. The database includes information (not for all the patients) on the sex, age, diagnosis and its grounding, anamnesis, comorbidity, therapy applied, and examination (coronary angiography, ventriculography, echocardiography, and circulatory dynamics). The records were processed using the software of the cardiac screening system PARCECG -6C. To convert the files from the WFDB-PhysioNet format of PTB database, the special program was developed. As a result, delimitation of the "Norm" and "Pathology" groups with sensitivity of 83,8% and specificity of 72,7% was obtained**.** According to the DM indexes analysis performed based on "THE PTB DIAGNOSTIC ECG DATABASE" of the German National Metrology Institute, the AMI is accompanied by increase in the microalternations of the whole QRS complex, especially in its terminal part, which can be associated with development of the myocardial electrophysiological nonhomogeneity. The maximum increase in the myocardial microalternation index and T wave alternation in the point $t_{maximum}$ was noted in Days 1-3 of the AMI and in the group with the VF-VT. The DM indexes: G5, G8 and TWA > 15 μV have the maximum diagnostic consideration in the group with the VF/VT.

DM Indexes of Acute Coronary Syndrome Patients

DM upon miocardial revascularization

By now, the first experience and DM method application results in coronary angioplasty *[34]*, *[77]*, *[78]*, *[86]* has been accumulated. The correlation between the coronary vessels damage severity and DM indexes change degree *[82]*, *[94]*, *[108]*, *[110]* was detected. It was established that the "Myocard" index parameters and microalternations cardiac cycle changed dynamically and can be used for estimating the vessels damage severity and analyzing the myocardial electrophysiological properties disorders in patients upon revascularization *[84]*, *[98]*. Y.Y. Bulgakova *[23]* recommended to apply DM ECG as a method of noninvasive estimation and diagnostics of the myocardial electrophysiological remodeling and prognosis of the disease course upon monitoring the patients with acute coronary syndrome at the different stages of hospitalization in the specialized cardiovascular care units. For more effective preventation of the remote unfavorable outcomes, the specific attention should be paid to the group of patients with the ACS, whose "Myocard" index exceeds the threshold value of 24%.

Regardless the positive influence of the revascularization, further course of the disease is mainly determined by the myocard damage origin degree and collateral blood flow adequacy. Therefore, the adequate noninvasive estimation being performed in the monitoring mode and including the electrocardiography methods of the myocard ischemic changes and energy metabolism are a clinically grounded necessity *[53]*.

According to Cruz-Gonzalez *et al.* *[2]*, upon examination of 101 patients, the DM technology implemented using the "PARCECG" allowed forecasting the angioplasty end results for the ACS patients by the G7+G9 indexes with (P=0.02) confidence. The analysis included the data of examination of 63 patients with the ACS examined at admission and in Day 1 after coronary angiography and operative therapy (the average age is 54,5±3,6 years). The 1st group included 36 (57%) patients, whose coronary angiography showed a vascular damage. The 2nd group included 27 patients with 2 and 3 vascular damage. The degree of stenosis degree in all patients was more than 50% and 87% patients had proximal damages. The control group included 47 conditionally healthy persons without any anamnestic and ECG indications of heart disease (av. age – 49,8±1,8 years). The patients with the severe course of diabetes mellitus, circulation failure higher than II by the NYHA (on the EF >40%), with high gradation arrhythmia and severe course of arterial were excluded.

In another study, the following main operation was performed: the transluminal coronary angioplasty; rarer, the mammary coronary artery anastomosis; coronary artery bypass surgery, and its variants. The MMI average values were higher on 2 and 3 vascular damage both, at admission, and after operational treatment in comparison with the data of the 1st and control group (23.3±0.5% and 21.5±0.3%). If the index values in the 1st group remained unchanged, they decreased significantly from higher values that reflected the therapy significant effect. The TWA_{max} index decreased definitely on the single vascular damage after the stenting on the 1st day from *15,0±0,7 μV* to *10.8±0.9 μV*. With 2 and 3 vascular damage, the MMI and TWA_{max} parameters on the patients' admission were higher, and after the stenting, only the MMI average values decreased to 21.5±0.3% *[94]*.

The QRS complex dispersion deviations (G3 и G4, *μV×msec*) and T wave (G5 и G6, *μV×msec*) indexes for the ACS patients on their admission before and after coronary angiography showed the maximum changes depending on the damaged vessels number in the repolarization period (G5 – *43.5±1.4* and *65.1±2.4 μV×msec*, G6 – *44.1±6.3* and 74.1±3.3 *μV×msec*) in the group with 2 and 3 vascular damage. Their average values were 3-4-fold greater than those in the 1st group and 10-fold greater than the standard values. It is also important to note the differences in the dispersion deviations existing in the QRS complex (G3, G4) in the group with 2 and 3 vascular damage. However, their increase compared to the 1st group and average values upon admission was manifested to a less degree. This data highlight once more that the degree of the remaining myocardial microcirculation and electrophysiological characteristics remains to be the key link defining the further state of patients and their long-term prognosis with adequate or even optimum results of the epicardial vessels angioplasty. As it follows from the data obtained, the dispersion amplitude maximum deviation indexes of the P wave (G1 and G2), depolarization symmetry (G7), and intraventricular conduction disorder (G8) in the examined ACS patients group, were detected in the group of patients with 2 and 3 vascular damage within the nearest postoperative period.

The obtained data on the MMI diagnostic consideration upon admission (at stage I of examination) as an index delimitating vascular damages 1 and 2-3, as well vascular damages 1 and 3, showed the sensitivity values of 85 and 93% and specificity of 36 and 36%.

As it was shown, in some cases according to the DM ECG, in the apparently healthy persons in satisfied state, the average normal values of the "Myocard" index increased and were close to standard values upon the acute Q-type MI.

These changes can reflect:

1) the states of the coronary microcirculation, microvascular resistance, and collateral circulation; in a less degree – epicardial arteries occlusion severity and regional perfusion heterohenity; myocardial circulation compensatory mechanisms and their exhaustion, as well as some accompanying metabolic changes leading to the myocardial electrophysiology characteristics

changes – ion channels functioning, membrane potential and affectability, electrical heterogeneity, etc.;

2) upon physical activity, functional tests, intraoperative obturations – coronary flow and collateral circulation reserve, metabolism integral characteristics and perfusion;

3) different cardial AI adverse events: the coronary arteries cramp, their dissection, acute occlusion, blood flow non-renewal phenomenon, anastomotic bursting.

The angiospasm can be developed both during angioplasty and in the first hours after the procedure and have generalized character and be observed outside of the areas of the instrumental impact. In the place of instrument impact, the angiospasm can be observed in 1–5% of the balloon angioplasty cases and, significantly more frequently, in up to 36% of cases when using other AI technologies. Thus, after the coronary angioplasty, the DM indexes reaction could be both, (+), and (–); as well as don't coincide by their terms, or manifestation degree. Its trend and manifestation should be determined by the origin state of organism and initial microalternation parameters, as well as compensatory mechanisms preservation.

Correspondently, the DM indexes negative reaction can be due to:

1) the simultaneous existence in the myocard of areas having different ischemic, metabolic, electrophysiology characteristics and dysfunction types, particularities of their localization;

2) variety of manifestation and functioning of the collateral circulation and microcirculation;

3) DM indexes individual deviations within the range of 3–7% during the monitoring of 5 minutes;

4) insufficiency of derivations number and ECG-signal amplitude deficit, intraventricular conduction disorders, etc. The different balance of these factors could determine both, the original data different variants, and DM indexes dynamics *[43]*, *[44]*, *[45]*.

DM Method Application for Monitoring of Angioplasty.

As you can see from our earlier works, exceeding the "Myocard" index "average standard values" takes place in a variety of cases between apparently healthy persons in satisfied state; it gives the results being close to the standard ones when the acute *Q*-type of MI exists *[2]*, *[108]*. In the first case, it could be the "diffuse myocardial changes" (in the standard electrocardiography terminology). In the second case, it could be the insufficient informational content of the limited number of derivations. In this regard, the dispersion mapping indexes estimation during the angioplasty (PCI) has been performed. The ECG-microamplitude results are displayed as a variance of digital dispersion characteristics and dispersion chart (cardiac portrait). The index reaction being measured with this instrument has been estimated for short-time balloon occlusions within angioplasty.

Now, the analysis of 22 angioplasties (PCI) has been performed. The dispersion characteristics measurement was being performed at the beginning of procedure, prior to each balloon dilation, after the dilation, and at the end of procedure. Starting the procedure was accompanied by the high level of the dispersion indexes (in 80% of cases), which significantly exceed the average standards and are subject to deviations.

Our conclusions concerning the above statistical estimations are as follows:

1) the dispersion criteria average values prior to the balloon dilation significantly exceed the same average values (T-test, N = 44, criterion G7+G9, $p < 0,03$) by 28% in average;

2) dispersion criteria average values at the balloon dilation intervals significantly exceed the same average values (by 35% in average) at intervals between the balloon occlusions (T-test, N = 232, criteria G7+G9, G9, $p \sim 0,035$); the dispersion heterogeny of the same samplings (F-test, criterion G9, $p < 0.1$) is an additional statistical grounding for this conclusion;

3) maximum indexes of sensitivity and specificity to the event of exceeding the dispersion criteria average values at the moments of balloon dilation amount to 72…84% (G9, G3-G9, N = 46) and 54…83%, respectively;

4) if one modifies the instrument algorithms based on the dispersion criteria logical addition, the expected maximum indexes of sensitivity and specificity to the event of exceeding the dispersion criteria average values at the moments of balloon dilation will amount to 91% and 83%, respectively.

Using the statistical hypotheses estimation procedures, we obtain the positive conclusion on the statistically significant average dispersion criteria reaction to the short-time inducted hypoxia arising on the balloon occlusion during the angioplasty. This reaction has the anticipated character, i.e., the average dispersion criteria at hypoxia exceed their values between the occlusions. Taking into account the balloon occlusion short-time character (~ 30 sec) and the powerful impact of vasodilating drugs during the angioplasty, these results evidence the high DM method sensitivity to the hypoxia.

In total, the results obtained evidence the intensive dynamics of the dispersion criteria during the angioplasty. The most significant changes both, increasing, and decreasing the dispersion criteria are observed during the two procedure stages – at the beginning of procedure and on balloons dilation. As it's established during the previous works that the dispersion criteria are high repeatable for the normal myocard, we can say that the dynamics observed reflects the actual electrophysiology amplitudes.

As it has been considered earlier, one of the most possible reasons of the "non-logical" (pseudopositive or pseudonegative) **changes** in the absolute values of DM dispersion criteria can **be**:

– the simultaneous existence in the myocard of the areas having the different ischemic, metabolic, and electrophysiology characteristics, as well as disfunctions and their localization particularities;

– multiple manifestation and functioning of the collateral circulation and microcirculation,

– different original state of the myocard and microalternation initial parameters;

– existence of the individual deviations and particularities of the myocard neurogenic and humoral regulating mechanisms;

– insufficient informative content concerning the number of derivations and ECG-signal "amplitude deficit" (ECGs of low amplitude);

– DM indexes deviation periodicity individual particularity in the range of 3-7% on monitoring during 5 minutes.

As the myocard dispersion characteristics high repeatability in the state of physiology standard is firmly established, these variations reasonably reflect the electrophysiology characteristics microamplitude at the initial angioplasty stages. No detailed reasons of these deviations are known today. However, we can suppose some influence of the pharmacy complex used according to the standard procedure, influence through the neurohumoral mechanisms of the introducer inserted into the artery, and impact of the radiopaque substances on selecting the coronary angiography optimum representation to be the reasonable hypothesis.

***DM Method Predictive Value for Patients with Acute Coronary Syndrome*.**

Influence of the IHD recrudescence duration to the remote outcome and "Myocard" dispersion mapping main index between the patients with acute myocardial infarction *[1]*, *[4]*, *[7]*, *[8]*, *[40]*, *[41]*, *[46]*, *[98]* has been studied. 47 healthy persons and 65 patients with the AMI (on 1st and 5th days) have been examined using the dispersion mapping method with the following analysis of the end points during the 1st year of monitoring *[45]*. The predictive value of the "Myocard" index of 24%, within short-term preinfarction (less than 1 day) on the lethal outcome analysis amounted to: sensitivity – 50% and specificity – 71%, with larger period (from 2 to 5 days) – 43% and 80%, respectively. The above study has shown that the lethal outcome rate is 2 times higher during a year of monitoring of the acute IHD short prehospital period.

The "Myocard" index was maximum on the 1st and 5th days of observation in a group with large terms of the IHD terms of recrudescence prior to the hospitalization (27,7±1,9% and 34,5±2,4% respectively). In this group, it's noted that it decreased from the 1st to 5th day and was maximum with larger terms of preinfarction period within the first day of examination in the hospital (30.7±1.9%), and on the favorable course of disease, the average values amounted to 19.3±2.0% by the 5th day. Significant increasing the QRS (G3+G4) complex dispersion deviations area was detected in a group with the favorable outcome on 1st and 5th day of disease with short preinfarction period (*470.2±21.3 μV×msec* and *476.0±22.9 μV×msec*) with insignificant changes of the ST-T (G5+G6) segment dispersion index deviations. In a group with the long prehospital period and rehospitalizations, the high values of these indexes have been noted by the 5th day (*450.7±18.9 μV×msec* and *422.8±22.4 μV×msec*, respectively). The most high average meanings of the segment ST-T (G5+G6) dispersion deviation on 5th day were in the 1st group for deceased persons with the recrudescence within 1 day (*408.5±22.4 μV×msec*). In addition, the stable increasing were noted in the group with the IHD recrudescence prior to the hospitalization from 2 to 5 days (*321.7±21.9 μV×msec* and *350.8±23.3 μV×msec*).

The T_{start} alternation indexes on the 1st and 5th day of the acute myocardial infarction were maximum in a case of unfavorable remote prognosis (*16. 2±0.8 μV* and *27.1±1.4 μV,* respectively), as well as $T_{maximum}$ values by the 5th day of disease (*31.3±1.2 μV*). The maximum increase the alternation values in the T_{start} and $T_{maximum}$ points was detected in Day 5 in the group with the remote lethal outcome. The predictive value of the $T_{maximum}$ > 27 μV alternation index on the 5th day of disease amounted to: sensitivity 71%, specificity 87% in Day 5 of the disease on the lethal outcome analysis.

In addition, the dispersion mapping indexes (G3+G4 and G5+G6) were studied in the groups of patients with the acute myocardial infarction. 47 healthy persons and 48 patients with the Q-type of AMI (on 1 and 20-25 day) were examined depending on their remote outcome and prehospital period duration. In the group with the favorable remote outcome, the maximum dispersion values have been detected in the QRS complex only with insignificant changes in the T wave. For a group with the lethal outcome (on the analysis within a year), the larger prehospital IHD recrudescence period has been characteristic. The stable high indexes of dispersion both, the QRS, and T wave have been noted by 5th day on the less than day hospital period and in the both points of examination (1 and 5 day) with prehospital period from 2 to 5 days.

Thus, the dispersion deviation maximum values have been detected in a group with the favorable remote outcome in a group with the short IHD recrudescence period prior to hospitalization and within the QRS complex only. For a group with the lethal outcome, the longer prehospital period of the IHD recrudescence has been characteristic, and stable high dispersion indexes of both, the QRS, and T wave have been noted by the 5th day preferably on the hospital period less than a day and in the both points of examination with the prehospital period from 2 to 5 days.

Myocard Microalternation Inexes upon Long-Term Monitoring

The study included the data on examination of 47 patients with the acute myocardial infarction (AMI), who were examined in Day 1-3 of the disease (the average age was 54.5±8.6 years)¸ who were monitored 91 times during 20…90 minutes *[44], [46], [56], [61]*. The MMI values were monitored and analyzed retrospectively, as well as analyzed dispersion groups (G1…G9), which were registered and calculated within 30 seconds periods consequently during the monitoring according to the electric microalternations technology. Based on the data obtained, for the AMI course without recrudescence (1st Gr.), the approximate proportionality of quicker (1.0-2.0 minutes) amplitudes and waves with the period more than 5 minutes (24%) was characteristic. In the 2nd and 3rd groups with the recrudescence or lethal outcome, high percent of the MMI amplitudes with the short period of 1.0-2.0 minutes was detected. At the same time, the wave percent with the period more than 5.0 minutes was higher than in the 2nd group on the recurring course. In a group with the non-cardiac reason of the lethal outcome, the percent of slow amplitude was high enough (18%) as well.

It was shown that long monitoring (from 20 to 90 minutes) of patients with the AMI detects the DM indexes of slow amplitude (in the first place of the MMI) with duration from 2-5 to 6-15 minutes, having indications of the flicker noise with the flicker noise (1/f) characteristics, which have been estimated as well *[56]*. It's known that 1/f processes include the wide class of different phenomena, e.g., changing the speed of chemical and biochemical reactions, potential difference variations at the neuromembranes, electrical noise in the nerve filament nodes of Ranvier, single unit and encephalon alpha-activity oscillations.

In addition, the monitoring has been performed for 3 anesthetized swines of 45-60 kg in the animals' artificial lung ventilation detecting the defibrillation threshold (DT), where the 20-secunds ventrical fibrillation (VF) is being eliminated using the bidirectional pulses *[55]*. The discharge doses from 70 to 150 J have been used. The study includes the data of 45 episodes of the VF-DP (91 discharge). We observed the similar in the experiment with cardioversion**.** It's shown: 1) on the DM microalternations amplitude indexes continuous registration between the anesthetized swines, the MMI wave amplitudes with the periods of 3-5 minutes and 10-12 minutes have been observed in the original condition; 2) the MMI amplitude with waves of 10-12 minutes are significantly longer than that of humane, achieving 70-90% in a variety of cases; 3) on the defibrillator discharges: a) the MMI amplitude decreases (in average by 10-12%, maximum by 30-40%,), and the number of episodes with wavelength of 2-3 minutes increases, б) stable structuredness of the MMI values is noted, which are parts of the slow amplitudes in ranges of 15-19, 23-28, 33-38, 43-50 and 60-70%; they repeat and form the above wave dynamics of the MMI amplitude changes.

It's possible that the microalternations change reflects the known universal mechanism of the myocard function alteration as a respond for the oxygen consumption non-correspondence to loadings of any genesis presented to the myocard. At that, if the current quick changes of the "beat-to beat" type are the variants of the quick adaptation changes, the DM slow wave amplitudes as the slowest heartbeat rate amplitudes shall be defined by the endocrinous and metabolic processes. It's obvious that there is a certain correlation between the 1/f characteristics and severity of the disease course, and flicker noise is a prospective instrument for its using as a method of the probable prognosis.

Conclusion

Taking into account the complicated demographic situation in the present Russia, the state policy is aimed at changing this situation by increasing the lifetime, performing the prenosological control and timely disease prevention for preservation of health of all the population groups. According to statistics, during the several decades, we will not able to decrease the main mortality causes in our country, *viz*., cardiovascular events. Organizing the Health Centers, which has started since 2009 according to the Order of the Ministry of Public Health and Social Development of the RF, is an important step in this regard. Preventive work with the population is the main task of the Health Centers; it is being implemented by the all year round screening of the population by appealability for detecting the persons with the excessive risk of the dangerous diseases. Monitoring the prevention effectiveness is performed for persons taking part in the health precautions. The screening is performed in the Health Centers, divisions of the prevention treatment, before-doctor offices in the polyclinics, etc. It is obvious that the main condition of timely detection of the cardiovascular individual risks on the prenosological diagnostics is covering the target population groups by the periodic effective screening. One of the main tasks of the Health Centers is screening the cardiac functional state and the earliest detection of the myocard electrophysiology status. The method implementing this task is the ECG dispersion mapping (PARCECG). Its purpose is to detect the early micropotential dispersion deviations in the ECG-signal, which can precede the pathology and be the ground and important for the cardiovascular diseases prenosological diagnostics. At that, it is necessary to understand that the "PARCECG" don't make the diagnosis being identical to the ECG-12 standard diagnostic technology. The method estimates the character and degree of the microalternation micropotential changes in the ECG-signal and represents the new ECG-diagnostics reflecting the current status of the electrophysiology remodeling and myocard compensatory resources reserve. The microalternation monitoring of the dispersion mapping ion characteristics has no analog due to absence of methods measuring it.

At that, we can note that the instrument meets the main requirements specified for the cardioscreening instruments as follows: performance function, *i.e.*, the checking procedure should not exceed 1-2 minutes with the preparing operations, and the procedure itself has no special preparing measures and is performed in clothes; its clinical results interpretation is available and demonstrative, and the output data interpretation time doesn't exceed 1 minute.

According to the multiple testing results, the instrument sensitivity and specificity on division the conditions "norm-pathology" amounts to 75...85%, i.e., these indexes are comparable with the average hospital diagnostic equipment indexes in regards with the differential diagnosis disease entities. The instrument value is comparable with the value of mass hospital instruments.

The application areas in the prenosological diagnostics are wide enough. They are: the screening on the population health survey; monitoring and control during the rehabilitation; adequacy analysis and selecting the physical exercises in the sport medicine; any situations requiring the myocard electrophysiology condition control, etc. Simultaneous usage of the simple functional samples significantly exceeds the diagnostic capabilities of the method. It's important to note that the DM indexes deviations detected having the high sensitivity and reflecting the myocard electrophysiology status disorder are not specific to genesis of the changes detected (ischemic, haemodynamic, metabolic, etc.).

The dispersion mapping method capabilities for detecting the ischemic changes have been studied in reasonable details. The average indexes of sensitivity and specificity of the instrument to the ischemia amounted to 79% and 76% respectively. For comparison, we could note the known low sensitivity of the resting ECG with 12 common derivations to the IHD, which according to the different sources amounts to 25%…50%. In addition, we could note some high reproductibility and resettability of result between the persons of different age, which allows estimating the myocard metabolism processes stability according to the DM in the different times and in the same time in the different days. The DM indexes individual particularities detected is preserved during the cardiovascular system stable state. The automated conclusion includes the information concerning the deviations manifestations, their probable course and recommended further actions.

Improving the population indexes by decreasing the premature disease incidence should be directed to the most correct detection of the persons having certain prenosological deviations and risks of the cardiovascular diseases. It will give the significant economy effect due to the early treatment value is 5 times lower than treatment value of the acute cardiovascular diseases during the first month only, and total expenses, including the rehabilitation stage and social payments are decreased 8 times.

The wide implementation of the DM method to the everyday medical practice allows the early detection of persons with the border-line or unfavorable myocard electrophysiology, risk groups of potentially dangerous arrhythmia, and adequate treatment and prevention.

Certainly, we need to understand deeper the relation between the ECG DM and electrophysiology of the above changes, their relationship with all spectrum of myocardial perfusion disorders (sleeping, constricted myocard and preconditioning), possible myocard regional perfusion heterogeneity and metabolic balance, as well as oxidative stress indications. Different variants of the stunned myocardium, including the hibernating myocardium, are considered now as a potentially arrhythmogenic substrate due to changing a variety of the electrophysiology properties. Therefore, we need improve the understanding of reasons and range of the DM microfluctuation indexes and their slow wave amplitudes.

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