The Estimation of Human Vital Signs Complexity

L. Bikulciene, E. Venskaityte, G. Jarusevicius

Abstract—Nonstationary and nonlinear signals generated by living complex systems defy traditional mechanistic approaches, which are based on homeostasis. Previous our studies have shown that the evaluation of the interactions of physiological signals by using special analysis methods is suitable for observation of physiological processes. It is demonstrated the possibility of using deep physiological model, based on the interpretation of the changes of the human body's functional states combined with an application of the analytical method based on matrix theory for the physiological signals analysis, which was applied on high risk cardiac patients. It is shown that evaluation of cardiac signals interactions show peculiar for each individual functional changes at the onset of hemodynamic restoration procedure. Therefore, we suggest that the alterations of functional state of the body, after patients overcome surgery can be complemented by the data received from the suggested approach of the evaluation of functional variables' interactions.

Keywords—Cardiac diseases, Complex systems theory, ECG analysis, matrix analysis.

I. INTRODUCTION

PHYSIOLOGICAL systems are capable of five kinds of behavior: equilibrium, periodicity, quasi-periodicity, deterministic chaos and random behavior. In order to obtain an integrated understanding of physiology, we require an understanding of the complex dynamics of physiological systems, [1]. The complexity of biological systems or the interrelations of its components even more, are difficult to understand without simplification of reality, so called mathematical modeling, [2]. Consequently, the fundamental nature of the cardiac signals and its measurement has caused the development of several new algorithms, [3]. The main limitations of mathematical modeling in biology arise from the very complexity that makes such modeling necessary, [4].

Cardiac disease is a complex phenomenon that involves remodeling at the level of the whole organism, the tissue, and etc. Each modification of the processes at these fractal levels is evidenced on the electrocardiogram (ECG). Moreover noninvasive analysis of cardiac signals provides real-time trending. Advanced nonlinear methods of measuring interactions of the cardiac parameters, derived from the mathematics of complex dynamics and fractal geometry have provided new insights into the abnormalities of cardiac behavior in various pathologic conditions. Two or more digital time series (in our case – ECG signals) contain information

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about the research object, and using certain mathematical methods this information can be expressed in the form of mathematical relationships. Our recent findings and research results of other scientists clearly indicate that these complex fluctuations exhibit interesting structures that were not previously anticipated. More importantly, these fluctuations may also contain useful information about the emerging complexity of the systems.

Thus, the research aim of this paper was to analyze individual intraparametric peculiarities of ECG data in high risk cardiac patients. The dynamical fluctuations of the signals obtained in complex biological systems in health or disease provide a unique opportunity to analyze the free running behavior of the integrative systems. As linear methodologies fail to provide significant information in conditions of extremely reduced variability (e.g. myocardial infarction) and in presence of rapid and transient changes the development of new nonlinear approaches seems to provide a new perspective and gives quite important results, [5].

Our proposed approach for the evaluation of functional state [6] includes the main functional systems of the body (cardiorespiratory, nervous and muscular systems) and it is applying in many our (group of scientific from Kaunas University of Technology, Lithuanian University of Health Sciences and Lithuanian Sport University) studies due to assess not only links between different dynamical processes and its changes, but also analyze them at different fractal levels as each level has its own complexity. The analysis of ECG parameters reflecting certain functional systems of the body recorded during procedure was analyzed by means of mathematical analysis methods based on second-order matrix analysis, which was developed in [7]. This method enables evaluation of the dynamic relationships of the system's parameters by cointegrating primary time series into the second order matrix. Also other nonlinear mathematical analysis methods and its applications are used regarding to solve a range of medical problems on quantitative basis for the proper use of the chaotic and spectral characteristics of ECG as noninvasive markers for cardiac mortality risk assessment and stratification in many cardiac dysfunctions. Although from the physicist's point of view the applicability of simplification and abstraction has been extremely successful in describing analyzed problems, it is still not clear, how similar analytical approaches can be successfully addressed to a living system. Moreover considering our present level of understanding, suggested models remain rather partial, therefore the great challenge is to use multiparameter perturbations to identify the safe areas, in which covariation of multiple processes supports the maintenance of stability [4].

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II. Modeling Biological Systems

Considering biomedical research, systems biology is an approach, which consciously combines reduction and integration of information across multiple spatial scales to identify and characterize parts and explore the ways in which their interaction with one another and with the environment results in the maintenance of the entire system. When large number of components are involved, the combinatorial problems arises, but more importantly it makes extensive use of mathematical modeling in order to represent and understand complex interactions of individual components or a whole biological entity [4]. Mathematical models based on nonlinear analysis methods play a complementary role to that of observation in all natural sciences [2]. Limited performance of linear models may be related to violation of the axiomatic presumptions about the data that are required by the model underlying the algorithm. Algorithms, which are based on linear stochastic models, presume the data variation is random and distributed around a mean, however, real data signals have internal correlations, are not random, and thus violate the model assumptions, thus time-dependent nonlinear algorithms that treat the problem of data nonstationarity show the greatest promise for clinical investigations [8].

A. The Model of Integral Evaluation of the Functional State

Because of the nonlinearity of the biological systems, it is unrealistic to achieve the goal of its comprehensive analysis purely by a traditional reductionist paradigm, therefore we applied innovative approach. Considering the dynamics of the human's functional state we employed a holistic approach, which comprises complexity, spatial and temporal fractal organization which remain invariant at different scales of observation, as well as nonlinear properties [9]-[11].

Our proposed model is developed in Lithuanian University of Health Sciences and it integrates the function of three main holistic elements (primary proposed by Vesalius in 1543, i.e.: P – periphery (executive) (the muscular system), R – regulatory system (nervous system), S – supplying system (cardiorespiratory system). Relation between these systems can be specified by several parameters, but usually we use the simplest and non-invasively estimated parameters – duration of RR interval, duration of JT interval, amplitude of ST segment, measurements of systolic (S) and diastolic (D) blood pressure, and duration of QRS complex.
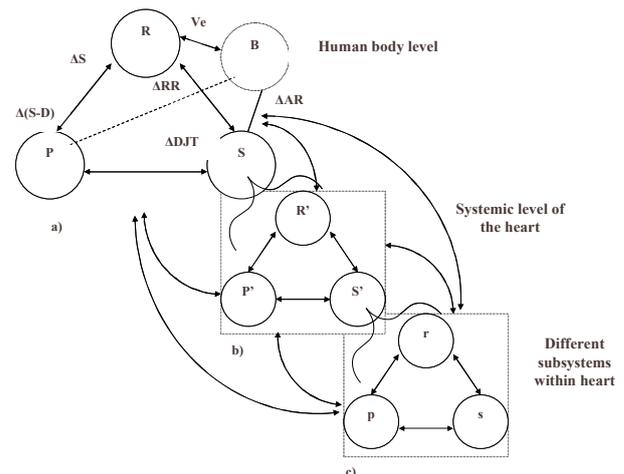

Fig. 1 Structure of the model of integral evaluation of the functional state, illustrating three fractal levels (Adopted from [11])

Here in Fig. 1 R – regulatory system, S – supplying system, P – periphery, ΔRR interval, duration of JT interval, amplitude of ST segment, measurements of systolic (S) and diastolic (D) blood pressure, and duration of QRS complex.

As was noted before, all objects in the natural world have features, which extend over many scales. Fractal complexity in time, such as seen in the heart rate (HR), is one example of this; it allows the system to repeat behaviors it has previously used. Chaos theory describes the underlying dynamics of the system, and chaotic behavior is also observed at many levels, from effector molecules in the cell to the heart function and blood pressure, [1]. For analyzing the interaction between different levels we combined our holistic approach with the idea of complexity profile suggested in [12]

Nevertheless, the major problem with fractal analysis is the lack of statistical tools, which can determine whether differences in the properties of fractal processes are significant, inasmuch as fractals have such bizarre statistical properties and this may require the development of a fundamentally new kind of statistics, [1].

B. Mathematical Analysis Approach

Traditional time series analysis techniques, partially described in [13], do not reveal the relationship between the indices recorded changes associated with the tested object multiscale (in mathematical terms - fractal) and chaotic structure, which allows to set short-and long-standing issues in structural and functional changes. Euclidian geometry fails to describe this because it can only deal with one scale at a time. Moreover biological systems may not remain in a single state long enough to gather the required amounts of data. Although bifurcations are easy to detect and do not require statistical analysis, but to detect more subtle changes in the attractor, a new statistical approach will be required. Another issue rises from self-similarity at multiple scales. It can also affect variance, because smaller fluctuations in the data are amplified as the resolution is increased regardless of whether this is due to the time or the sample size increase and tends towards infinity. This poses fundamental problem to the approach of

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statistical hypothesis testing, because there is no true mean of the system and, if we wish to look for changes in the state of a fractal system, we cannot use our existing analytical tools because they are essentially blind, [1].

Comparing traditional statistical analysis methods and mathematical analysis methods these two different analytical methods, it is possible to distinguish that statistical analysis methods more applicable to global processes of the body and requires a large amount of information and analysis of the mathematical methods used to analyze the local processes of the body and thus do not need such a large amount of information, [14], [15]. However, non-linear and non-stationary signal analysis is not enough conventional methods. Traditional time series analysis methods fail to reveal the changes of interactions of the recorded indices associated with the investigated object's multiscale structure and instability in the dynamics, which allows the issue of temporary or long-term structural and functional changes. In the literature so far modern methodologies mainly applied on heart rate variability analysis [16], [17]. The same analytical methods (mostly – probability) is designed for the analysis of rapid and slow processes, but not for the interaction between systems. Interactions of local complex adaptive system (CAS) components, which requires exploring the processes of discovery and examination at a multiscale levels, opens the door to the global processes of the specific models or helps to predict the behavior of the global nature.

Signals dynamic interactions, characterizing individual systems, are very significant to the human body, as CAS, functions' analysis. Parameters identification, method sensitivity analysis and the understanding physiological significance of final results still remains an actual problem, [18], [19]. Non-linear mathematical analysis methods and application integration, solving a range of medical and sports science problems can be one of those solutions.

The full potential of fractal mathematics and chaos theory remain to be realized, and await further development, although these concepts have already provided revolutionary insights into the nature of the living things [1].

There the method designed for extracting "hidden information" in time series generated by complex living systems and based on the matrix theory and has been proposed and developed in [7], considering the inter-parameter relationships obtained during monitoring of vital signals.

For the investigation of interaction between two objects, two synchronous numerical time series ($x_n, n = 0,1,2, \dots$ and and $y_n, n = 0,1,2, \dots$ representing the exploratory object are formed, in which x_n and y_n are real numbers and they represent the recorded ECG parameters. When elements of the series are determined variables, information about the object of investigation is described using special mathematical equations [20].

From the given numerical time series $x_n, n = 0,1,2, \dots$ and and $y_n, n = 0,1,2, \dots$ the matrix time series $A_n, n = 0,1,2, \dots$ the can be formed

$$A_n = \begin{bmatrix} x_n & a(x_{n-1} - y_{n-1}) \\ b(x_{n+1} - y_{n+1}) & y_n \end{bmatrix}, \qquad (1)$$

where parameters are dependent on properties of time series. In the simplest case, the coefficients can be equal 1. The elements of matrices can be formed in a more complicated way also. Though different methods for data analysis can be applied, in this investigation of matrix time series, the numerical characteristics of the second order matrices and the main components of the matrix (1) were used, i.e.:
$\text{Tr}A_n = x_n + y_n$ (trace), $\text{dfr}A_n = x_n - y_n$ (difference), $\text{cdp}A_n = ab(x_{n-1} - y_{n-1})(x_{n+1} - y_{n+1})$ (co-diag product),

From these initial parameters follow characteristics which have more applicative sense:

$$dskA_n = (dfrA_n)^2 + 4cdpA_n \text{ (discriminant)}, \qquad (2)$$
$$\lambda_{1,2} = \frac{1}{2}\left(TrA_n \pm \sqrt{dskA_n}\right), \text{(eigenvalues)}.$$

All these characteristics can be used in data analysis, but in this research the results with determinant will be proposed.

In order to avoid noise influence, the elements can be averaged. It must be noticed, that if a number of terms in the sums increase, the sequence of discriminants (dsk) becomes smoother, but its character remains the same. From numerical investigation, it is obtained that changing of parameters a and b exerts influence only on the amplitude of the sequence, but not on its character, and therefore in further calculations the simplest mode of the matrix formation was used. The initial data were normalized using minimal and maximal physiological values of the recorded parameter.

Complexity measure, reflecting the degree of coupling between variables, was expressed as the value of discriminant, (2). If the value of discriminant decreases and is close to zero – the interaction between two synchronous numerical time series (ECG signals) increases, but the complexity of the system decreases. The proposed methodology is suitable for various types of signals. In addition, to establish the relationship between two or three signals only three points are required: past, present and future, [11].

III. THE APPLICATION OF DEVELOPED METHODOLOGY

By observing the degradation of dynamical complexity in disease and aging, one realizes that life-threatening pathologic of the whole system, or a strong "mode-locking" among them. In contrast, a healthy biological system usually displays intermittent coupling between its sub-systems. Each component of the system may engage and then disengage with other components of the system. This type of on-and-off "cross-talk" between different parts of a complex system (reminiscent of how different instruments are integrated together in a symphony orchestra) seems to be a prominent characteristic of healthy biological function.

One of the major public health problems, which is highly related to mortality is cardiovascular diseases. Cardiac ischemia is associated with typical alterations in cardiac biosignals that have to be measured, analyzed by mathematical algorithms and allegorized for further clinical diagnostics. The

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fast growing fields of biomedical engineering and applied sciences are intensely focused on generating new approaches to cardiac biosignal analysis for diagnosis and risk stratification in myocardial ischemia.

A. Material and Methods

Functional adaptation features and their homogeneity can be investigated using cointegration of two time series taken from ECG monitoring during different states of the body (rest, physical workout etc.). Previously mentioned method was also tested in various groups of subjects (athletes, non-athletes, patients with different diseases, etc.). In this paper we present the results of the group of 24 subjects with an average age of 64.6 ± 1.09 yrs; stature – 1.6 ± 0.02 m and mass – 87.7 ± 5.75 kg, who were hospitalized in the Lithuanian University of Health Sciences Hospital, Cardiology clinic. Recanalization treatment was applied for all patients.

All the investigations were approved by the Ethics Committee of Biomedical Research of Kaunas University of Medicine (Protocol No. BE-2-27).

The ECG parameters in 12 leads of continuous monitoring were recorded by using computerized ECG analysis program "Kaunas-Load" (developed at the Institute of Cardiology, LUHS, Lithuania). This computerized program was used in many studies of our researchers group, for instance in research [7], [10], [11], [15], [21] etc.

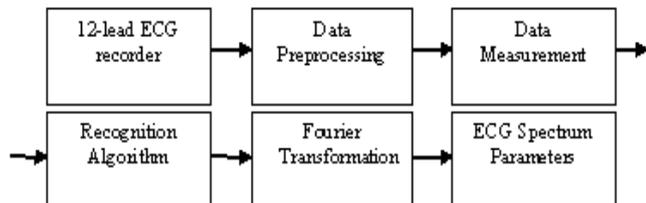A structure of ECG recording equipment "Kaunas-Load" is shown in Fig. 2.

Fig. 2 Structure of ECG recording equipment "Kaunas-Load" (Adopted from [21])

Signal discretization rate was 500 Hz. In this work three ECG parameters of each cardiocycle were analysed, taken from the II lead (RR interval) and the V lead (JT interval and QRS complex):

1) RR interval (ms) – it is an interval between two one after another following R waves, which indicates the time interval between two heartbeats. A total body functionality can be described according to RR interval and in particular – regulatory processes also it is describing systemic level of the human body;

2) JT interval (ms) – the interval from the ECG junction point J to the T wave end, which characterizes duration of ventricular repolarisation (sub-systemic cardiac metabolic changes).

3) QRS complex (ms) – the duration of this complex illustrates the spread of excitation in the heart, describing the cardiac activity of the inner regulatory processes (sub-systemic level).

Considering the impact of the hemodynamic restoration procedure on functionality of the human body in patients with MI history, the recorded ECG was divided into following stages: 1st - before Recanalization procedure, 2nd - during Recanalization procedure, and 3rd - after Recanalization procedure.

A statistical difference was tested by applying the nonparametric Mann-Whitney test for independent samples and the nonparametric Wilcoxson test for related samples (software SPSS for Windows 17.0). Difference, with respect to error probability less than 0.05, was pointed as statistically significant.

B. Results and Discussion

In order to evaluate a dynamic state over multiple points in time, we are demonstrating the application of the proposed methodology in an example of high risk cardiac patients, although it can be extended to other domains where predictions based on time-series data is needed.

Short-term coronary blood flow disorder induces myocardial ischemia, which causes decrease of the biochemical and enzymatic processes, i.e., impairment of myocardial nutrition. Denervation of the heart increases the fractal complexity of the heart rate (HR), indicating that the fractal complexity has its origin in the heart itself, and is modulated by the autonomic nervous system [22], [23].

Dynamics of RR (Heart Rate) interval for subject A.S. before recanalisation, during procedure and after it is presented in Fig. 3.
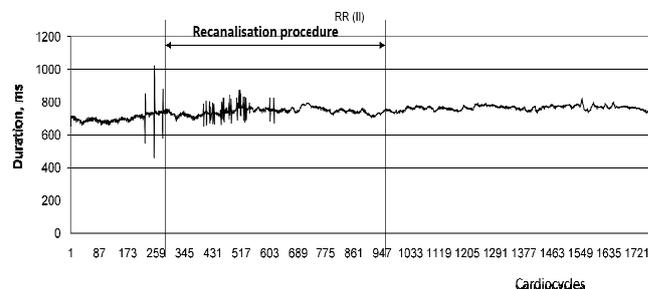

Fig. 3 The impact of the hemodynamic restoration procedure on HR

In Fig. 3 it is shown the emergency of the reorganization in the heart's regulatory system and the stabilization of the parameter after the procedure. Although time series of the signals provide information about the system, but only abrupt changes can be detected by averaged data (which is necessary for the common linear methods) and also if only the amount of the data is sufficient.

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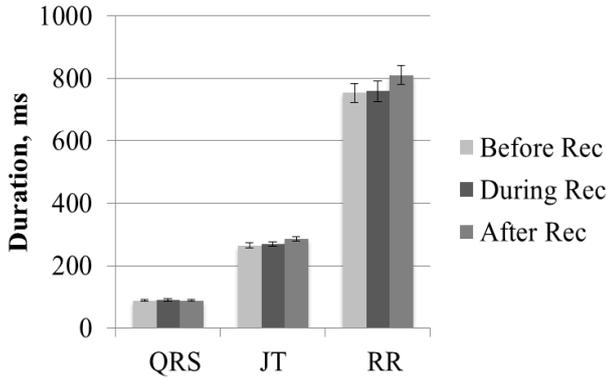Vol:8, No:1, 2014

Fig. 4 Length of complexes during experiment

Figs. 4 and 5 illustrate this problem, when analyzing separate indices it is possible to identify the tendency of the dynamics of the particular part of the system. Also this data is valid only if it is taken into account the decomposition of the complex system in order to analyze it, i.e., the interrelation within the system is excluded.

Prolonged JT interval duration during procedure and after it, suggests the slowdown of the repolarization and slower metabolic reactions in the heart [24].
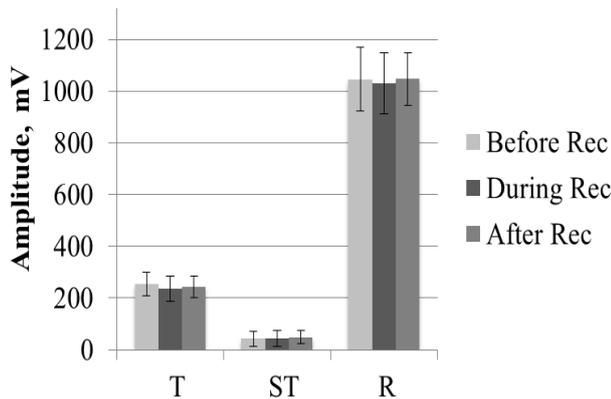

Fig. 5 Amplitudes of complexes during experiment

Analogically increased the duration of RR interval, which lead to the activation of the regulatory system of the heart and causes the changes in metabolic processes accordingly. However, the analysis of duration and amplitude of the separate characteristics didn't revealed statistically significant differences in comparison of the stages Figs. 4 and 5.

Therefore nonlinear mathematical analysis methods and its applications are used regarding to solve a range of medical problems on quantitative basis for the proper use of the chaotic and spectral characteristics of ECG as noninvasive markers for cardiac mortality risk assessment and stratification in many cardiac dysfunctions in future. This signals time lines cointegration method was used to compared relationships of the ECG parameters, when ECG was recorded for healthy individuals and patients before the coronary angioplasty procedure (relieve of blood vessel blockages) and after it. This data revealed that the values of the interparametric relationship were higher in healthy individuals compared to

patients.

Interaction of RR and JT intervals for subject A.S. before recanalisation, during procedure and after it is presented in Fig. 6.
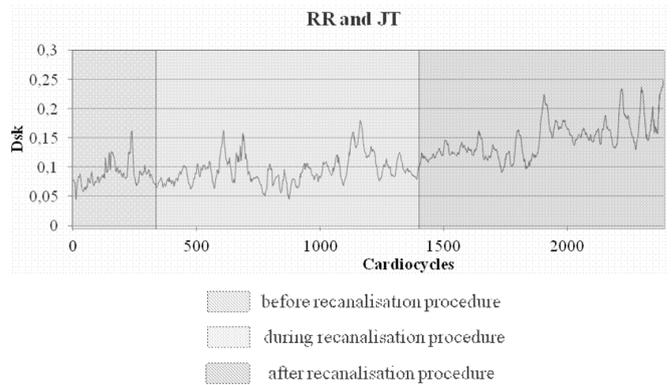

Fig. 6 Dynamical changes of interactions of ECG parameters

The interaction of RR and JT intervals revealed increasing oscillations and increasing values of the discriminant, which is the confirmation of the reorganization of the complex system in the systemic level. These dynamical changes of the interaction between RR and JT intervals also coincide with the processes, which were obtained in [24]. In this study was shown, that instantly after Recanalization and during following 24 hours in all the investigated patients' prolongation of JT intervals was obtained.
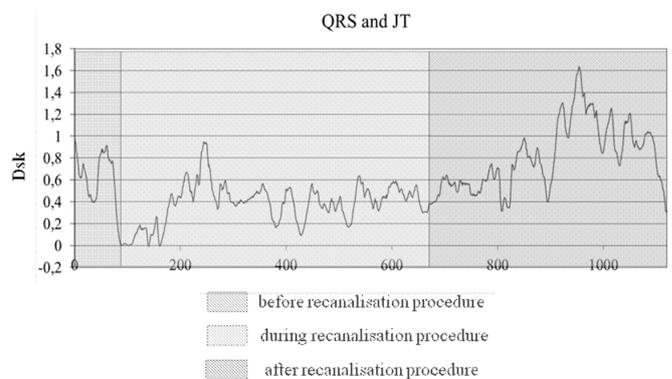

Fig. 7 Dynamical changes of interactions of ECG parameters

Even more pronounced bifurcations from one stage to another were observed in the subsystemic level of the system (QRS and JT interaction). In accordance with other authors [11], [14] obtained tendency suggest that essential more pronounced ischemic processes occur in the deeper levels of the cardiac system at the onset of hemodynamics restoration procedure.

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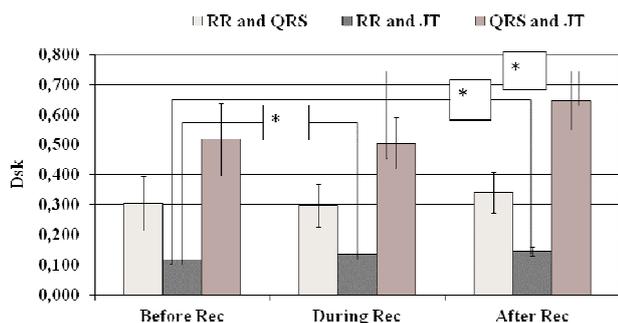International Journal of Computer and Information Engineering
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Fig. 8 Dynamical changes of interactions of ECG parameters

Notations in Fig 8: Rec – Recanalization procedure, Dsk – discriminant, * - statistically significante difference (P ≤ 0.05).

During analysis of averaged data, statistically significant difference (P ≤ 0.05) were observed in the interaction of RR and JT intervals comparing the stages before recanalization and during procedure, and before recanalization and after it. Also were obtained statistically significant difference (P ≤ 0.05) of the interaction between QRS complex and JT intervals, comparing the stages during recanalization and after it (P ≤ 0.05).

Peculiarities of evaluation of ECG indices interactions show the exposure of the body's functional changes at the onset of hemodynamics restoration procedure. The suggested method confirmed the changes of the repolarization during Recanalization procedure, which is related with ischemic myocardial lesion. Therefore the evaluation of the interactions of physiological signals by using matrix analysis is suitable for observation of functional state of the body.

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