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Risk Method Assessment Of Coronary Heart Disease In Carriers Of Polymorphic Cardiogenic.

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ABSTRACT

Due to the high prevalence of cardiovascular disease (CVD), including coronary heart disease (CHD) additional risk factors based on molecular genetics are currently explored. It is believed that the structure of the body and processes occurring in it are defined by a set of DNA of genes. It should be noted that each individual set of human genes and the DNA structure is not the structure of the absolute list of factors predetermine imbalance in these growth processes, but their role is very high. It is known that during the occurrence of different mutations, gene structure may be changed by substituting some amino acids by others. Thus, a gene polymorphism, and carriers of the same gene with a different set of amino acids may have a different risk of developing coronary heart disease. It follows that the genetic analysis reveals the individual predisposition to the emergence of genetically determined risk factors. The article is devoted to the development of a new method of assessing the current state of the cardiovascular system, as well as the degree of risk of CHD based on modern virtual information technology acquisition and processing of various types of cardiac data, including the results of the analysis of cardiogenic affecting the development of risk factors. Technical solution proposed by a team allows for remote monitoring of the patient's CVS through telemedicine technologies with portable Cardiosensor for transmission, processing and storage of information in databases (DB) "ARM-Cardiologist"; to develop managed care decision based on the generated program CHD diagnosis based on proposed set of diagnostic features CVR status, provide information support to the cardiologist for diagnosis using the "ARM-Cardiologist" reference system; improve the accuracy of early diagnosis (risk of) cardiovascular diseases and carry a warning on the classification of patients at risk for coronary heart disease from birth based on the results of genetic analysis.

Keywords: cardiology, coronary heart disease, heart electronic model, polymorphism cardiogenic, decision support system, coronary heart disease risk factors, cholesterol.

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INTRODUCTION

Over the past few decades we have been intensively studied causes of cardio - vascular disease [1]. Since the classic risk factors are not fully predict disease are being sought additional risk factors based on molecular genetics [2-4]. Poslednie advances in molecular biology have allowed detect multiple gene polymorphisms [5, 6] associated with lipid metabolism, the renin-angiotensin-aldosterone system and the adrenergic, insulin resistance, oxidative stress and endothelial dysfunction, inflammation and thrombosis, that may have adverse effects on the cardiovascular sistemu.Vyskazana the hypothesis that multiple polymorphisms in the presence of environmental factors may act synergistically in the pathogenesis of atherosclerosis and coronary heart disease and cause of polygenic and multifactorial zabolevaniy.Individualny coronary risk may be associated with the presence of a critical accumulation of harmful polimorfizmov.Takim, the carriers of the same gene with a different set of amino acids may have a different risk of developing coronary heart disease (CHD).

The complete sequencing of the human genome in the program "Human Genome" was completed in 2003. HapMap study allowed the identification of genes and gene markers for heart disease and other diseases. There is the prospect of creating a universal data bank, including information about the mutations that lead to multifactorial disease. With this idea and made by Richard Cotton Hague Kazazyan, giving the name of the project «HumanVariomProject». At the moment, there are more than 150 genes, polymorphic variants which are associated with a predisposition to cardiovascular disease (CVD).

The identification of these groups of genes and their association with other groups, constitute the scientific basis for predictive medicine. Testing allelic variants can get enough objective information about the condition of a metabolic system of the body, to assess disease risk and apply appropriate preventive measures [7].

The need for early diagnosis of coronary artery disease and the pursuit of the validity of medical decisions dictated by the urgency of wide introduction in medical practice of monitoring the condition of patients with coronary artery disease with the help of the automated systems of telecommunication. Currently, a group of authors developed an intelligent system "ARM-Cardiologist" for solving the problem of the generation of the electronic diagnosis of CHD. At the same time, it was calculated conditional probability of having coronary artery disease as a result of the analysis of the patient's cardiovascular system. In connection with the transition to the level of gene diagnosis of risk factors for disease, such as coronary heart disease, the amount of information to be processed doctor increased substantially. This necessitates the use of hardware and of software systems in the workplace physician. That, in turn, will contribute to the realization of high-quality care to patients.

Objective: to develop a new method of assessing the current state of the cardiovascular system, as well as the degree of risk of CHD based on modern virtual information technology acquisition and processing of various types of cardiac data, including the results of the analysis of cardiogenic affecting the development of risk factors.

RESEARCH METHODOLOGY

Table 1 illustrates the possible genes and their mutations indirectly affect the development of coronary heart disease.

Table 1: Significant gene mutations that increase the risk of coronary heart disease

Regulated processes	Gene	Type of mutation	Alleles
Arterial hypertension	AGT	M235T T174M	
	ACE	c.2306-109_2306-108ins288	D/D
	NOS3	c.582+353_379del	
hypercholesterolemia	APOE	C112A	E2/E2
		A158C	

Blood coagulation and fibrinolysis	ITGA2	C807T	
	GP1BA	T145M	
		1234_1272del39/ins39	
	ITGB3	c.176T>C	
	FGB	c.-4676G>A	
	F2	G20210A	
	F5	A506G	
		Leiden mutation	
	MTHFR	C677T	
		A1298C	
	MTRR	I22M	
	MTR	A191G	
	PAI-1		4G/4G
Inflammatory biomarkers (especially high-sensitivity C-reactive protein (CRP);	C1444T		T T/T
Interleukin 6 (IL 6)	G174C		G/G
Tumor Necrosis Factor	A	A308G	

In recent years, various groups of scientists studies have been conducted, in which they determined the risk of coronary heart disease in carriers of certain genes (Table. 1).

The gene AGT Allel T174M

A group of researchers have shown that the population of the Rostov allele carriers M and TM genotype have an increased risk of developing coronary heart disease (OR = 3.56 and 2.53 resp.), While carriers of T allele and genotype MM - reduced risk

(OR = 0,28 and 0,39 resp.) [8].

The gene AGT Allel M235T

A group of researchers have shown that the population of the Rostov allele carriers M and TT genotype have an increased risk of developing coronary heart disease (OR = 5.50 and 2.59 resp.), While carriers of T allele and genotype MT - reduced risk (OR = 0.18 and 0.39, respectively.) [8].

ApoE gene in association with other genes.

Genotype risk of CHD are associated with atherogenic dyslipidemia s4 allele ApoE genotype 4G / 4G PAI-1 gene and the C allele of the GPIIIa gene T196S, increasing the risk of blood clots, and A allele gene UCP2 G866A, associated with insulin resistance and oxidative stress. The odds ratio for CHD for these genotypes ranged from 1.54 to 1.73 with an average of 1.67 after adjusting for traditional risk factors [9].

JJCP gene G866A allele 2 in association with hypertension

This combination has the effect of synergy of risk factors. In this situation, the odds ratio for CHD of 2.38 (1.53 in the control group, $p < 0.05$) [9].

The gene ApoE E4 allele in association with smoking

This combination also has a synergy that increases the risk of coronary heart disease. This odds ratio of 1.45 (1.17 in non-smokers, $p < 0.05$) [9].

PAI-1 gene allele 4G / 4G in association with smoking

This combination also has a synergy that increases the risk of coronary heart disease. This odds ratio of 1.88 (1.59 in non-smokers, p <0.05) [9].

The dynamics of changes in blood levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor (TNF) [6] may reflect processes occurring in atherosclerotic plaques and coronary artery [10]. However, the concentration of inflammatory markers in blood depends on genetic factors influencing the transcription levels of individual genes. Thus, for CRP gene described several polymorphic sites, for certain allelic variants and genotypes which are characterized by increasing the level of CRP in blood plasma [11]. In particular, in the case of C1444T polymorphism in the 3'-untranslated region (3UTR) gene and the T allele carriers genotype T / T observed increase in CRP levels [11]. For IL-6 gene (IL6) also known polymorphic variants affecting the IL-6 level in the blood. Genotype G / G polymorphism G (174C), located in the promoter region IL6 gene associated with higher levels of IL-6 in plasma [12]. Polymorphism A (308) G gene TNF, also located in the promoter region influences the transcription and synthesis of proinflammatory cytokines [13].

Coronary heart disease, due to its multifactorial, requires a broader consideration of the general state of health. It contributes to the prevention, early diagnosis and successful treatment of a patient. To facilitate the consideration of all the information that the doctor can collect for a limited period of time created software "ARM cardiologist." Generation of health management solutions (HMS) based on the analysis of diagnostic signs of coronary artery disease is one of the main procedures performed according avtomatizirovannymintelektualnym workplace. For each attribute in the software package provides a weight rating feature for a particular patient on the basis of an analysis of its health. According to the authors, this software package enhances the reliability of early diagnosis [14].

RESULTS AND DISCUSSION

This article presents a method developed by a group of authors and implements its hardware-software complex "ARM-Cardiologist", whose main purpose is the generation of electronic diagnosis as a medical project management solutions.

Structural and functional diagram of an electronic model of the heart of said hardware and software system is illustrated in Fig. 1 [14, 15].

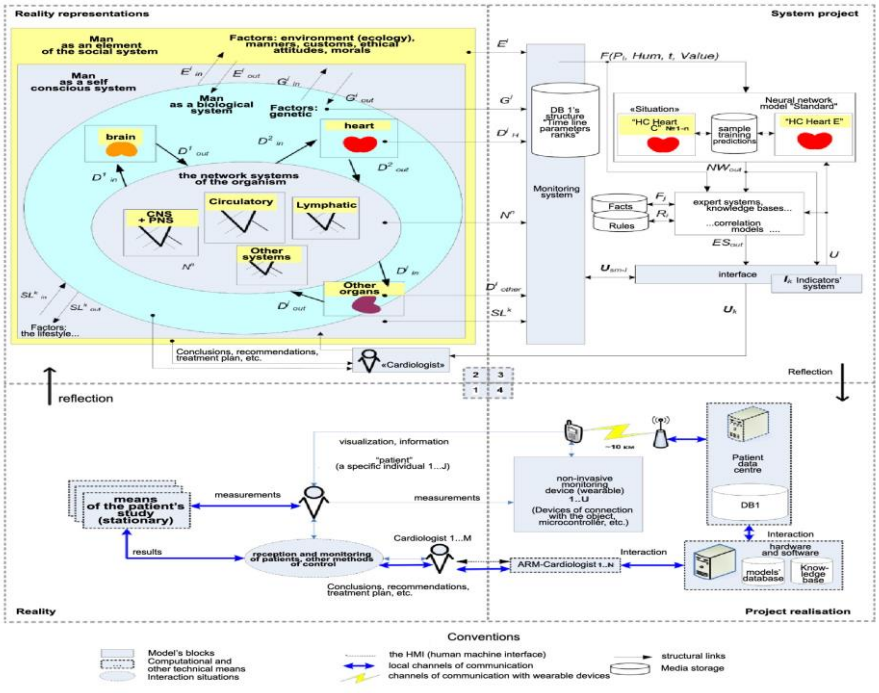

Fig. 1. Structural and functional diagram of an electronic model of the heart

The scheme consists of four functional modules, interconnected by a principle of "reality - representation of reality - the reality of project changes - implementation of changes," which allows us to describe the various aspects of the functioning of the cardiovascular system (CVS). We give a brief description of the role and place of each of the functional modules in the solution of the main task - developing electronic project diagnosis.

Module 1 describes the interaction of the situation, "the cardiologist-patient" prevailing at the moment. The situation is characterized by the traditional episodic periodic interaction occurs when the patient's complaints and conducting preventive and (or) maintenance treatment. The use of the permanent remote control means is provided by module 4.

Module 2 is a model of CVS within view of man as a hierarchical management system, consisting of several interconnected contexts: the first (I) - the human context as the biological system; the second (II) - the human context as self-conscious system, comprehensive context I; the third (III) - the human context as a social element of the system, comprehensive context II.

Module 3 contains a model of a system consisting of multiple related blocks: Block 1 - a database; Block 2 - Monitoring System series of parameters for each patient; Block 3 - the interface between the "cardiologist" and monitoring system (Block 2), and the other blocks of the system; Block 4 - a set of models of the "stimulus-response" allowing "learn" on the data observations and predict the possible response to different combinations of influencing factors in "real time"; Block 5 - a set of models based on the mathematical methods (correlation model and the like) and expert systems techniques; Block 6 - model "cardiologist", implementing methods for supporting decision-making. Purpose of this module - information support of decision-making by the cardiologist and the subsequent development of managed care solutions in the form of an electronic project diagnosis.

Module 4 - contains the implementation of the system to specific software and hardware, allows remote monitoring of the patient's cardiovascular system. It consists of five blocks of honey are communication channels (both local and global assignment): workstation cardiologist; server models; data center on the parameters of a patient's state; private mobile device noninvasive testing (in an amount sufficient to service the needs of a predetermined number of patients); Data transmission system between mobile devices and fixed access point.

The calculations of the conditional probability of having coronary artery disease as a result of the classification of the cardiovascular system of a patient by groups of diagnostic features, including genetic analysis of polymorphic genes CHD were carried out. The example of forming training sample based on statistical analysis of medical data was described. There was the evaluation of the effectiveness of e-diagnostics on the results of clinical trials (653 people).

The analysis generated by the program "ARM-Cardiologist" electronic diagnosis leads to the conclusion that the probability of a correct diagnosis of the presence of coronary artery disease in a patient, taking into account the polymorphism of cardiogenic equals 91.1%. It is shown that the probability of erroneous diagnoses sgenirirovannyh sostavlyaet 8.9%.

Thus, clinical studies confirmed the performance of the intelligence system "ARM-cardiologist and showed the possibility of accurate diagnosis of the presence of coronary artery disease in a patient with it. The results of the genetic analysis carried out at any time of the patient's life, allow them to enter his personal electronic cardio case history that will enable the classification of warning patients of CHD risk groups more at birth and will help the cardiologist to predict the process of developing coronary heart disease, to take appropriate preventive measures.

CONCLUSIONS

Proposed by a team the technical solution of hardware and software complex "ARM-Cardiologist" allows you to:

1) to carry out remote monitoring of a patient CVS through telemedicine technologies with portable Cardiosensor for transmission, processing and storage of data in databases (DB) "ARM-Cardiologist";
2) to develop managed care decision based on the generated program diagnosis of CHD based on the proposed set of diagnostic features CVS status;
3) to provide information support to the cardiologist for diagnosis using the "ARM- Cardiologist " reference system;
4) to improve the accuracy of early diagnosis (risk of) cardiovascular diseases and carry a warning on the classification of patients at risk for coronary heart disease from birth based on the results of genetic analysis.

CONCLUSION

The study showed the possibility of use in medical practice a new method of assessing the risk of CHD. Implementation of the proposed team of authors of the new technical solutions will improve the accuracy of early diagnosis of cardiovascular diseases and to carry out a warning for the classification of patients at risk for coronary heart disease from birth based on the results of genetic analysis. This would allow for preventive treatment and allow mortality reduction in patients with coronary artery disease.

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