NEW TECHNIQUES AND MODELS FOR ASSESSING ISCHEMIC HEART DISEASE RISKS

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The paper focuses on tasks of creating and implementing a new technique aimed at assessing ischemic heart diseases risk. The techniques is based on a laboratory-diagnostic complex which includes oxidative, lipid-lipoprotein, inflammatory and metabolic biochemical parameters; s system of logic-mathematic models used for obtaining numeric risk assessments; and a program module which allows to calculate and analyze the results. we justified our models in the course of our research which included 172 patients suffering from ischemic heart diseases (IHD) combined with coronary atherosclerosis verified by coronary arteriography and 167 patients who didn't have ischemic heart diseases. Our research program included demographic and social data, questioning on tobacco and alcohol addiction, questioning about dietary habits, chronic diseases case history and medications intake, cardiologic questioning as per Rose, anthropometry, 3-times measured blood pressure, spirometry, and electrocardiogram taking and recording with decoding as per Minnesota code. We detected biochemical parameters of each patient and adjusted our task of creating techniques and models for assessing ischemic heart disease risks on the basis of inflammatory, oxidative, and lipid biological markers. We created a system of logic and mathematic models which is a universal scheme for laboratory parameters processing allowing for dissimilar data specificity. The system of models is universal, but a diagnostic approach to applied biochemical parameters is specific. The created program module (calculator) helps a physician to obtain a result on the basis of laboratory research data; the result characterizes numeric risks of coronary atherosclerosis and ischemic heart disease for a patient. It also allows to obtain a visual image of a system of parameters and their deviation from a conditional «standard – pathology» boundary. The complex is implemented into practice by the Scientific Research Institute for Therapy and Preventive Medicine.

Key words: risk assessment, ischemic heart disease, laboratory and diagnostic complex, biochemical parameters, logic and mathematic model, program module, questioning as per Rose.

According to statistics, each thirteenth RF citizen suffers from cardiovascular pathology; ischemic heart disease plays a leading part among mortality causes related to circulatory system diseases (55.7%) [1]. Mortality as per ischemic heart disease (IHD) in Novosibirsk region amounts to more than 35 people per 1,000 adults [6]. In relation to that, any research aimed at improving diagnostics and making it timely as well as secondary ischemic heart diseases prevention is of specific importance within strategies of providing medical assistance to cardiologic profile patients [1, 8, 11]. The

Ó Yakovina I.N., Bannova N.A., Kashtanova E.V., Polonskaia Ya.V., Ragino Yu.I., 2017

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urgency to study factors and biological markers of key pathophysiological mechanisms of cardiovascular diseases evolvement in West Siberia region is determined by its specific climatic and geographical conditions, nutrition peculiarities, and extremely high prevalence of ischemic heart disease risk factors; therefore, it is necessary to obtain new data on risks of the disease complications and on ways of improving its early diagnostics [9].

Cardiovascular risk is a probability of any unfavorable event occurrence in cardiovascular system (including death caused by a cardiovascular disease or its complication) within a certain period of time (for example, within the next 19 years) [15]. Risk stratification in IHD diagnostics is performed on the basis of clinical data, stress-tests results, heart ventricles functioning assessment, coronary arteriography results, and other parameters [7, 10, 14, 18].

SCORE scale is widely known among risk meters which are used in cardiology; this scale is aimed at assessing absolute risk of a fatal cardiovascular disease within the next 10 years. When risk is assessed as per SCORE scale, its assessment allows for the following parameters: sex, age (40-65 years), blood pressure, crude cholesterol level, and smoking state [13]. Cardiovascular risk is also assessed depending on optimal values of lipid parameters, body mass index, and metabolic syndrome diagnostics results [4, 16].

As a rule, assessment of a fatal cardiovascular disease risk is made via summing points received as per each risk meter scale parameter. The obtained result is then converted into per cents or remains in numeric values. After that, to determine risk degree, it is necessary to use look-up tables containing values obtained as per a risk meter scale and probability of fatal cardiovascular diseases occurrence or evolvement given in per cents. Such techniques and procedures for analyz-

ing values of parameters which are included into risk scales are present in most well-known scales such as HAS-BLEND, CHA2DS2-VASc, GRACE, CRUSADE, and TIMI. Risk assessment can also be performed by assessing a parameter occurrence within a range which a certain risk degree corresponds to. A fatal cardiovascular disease risk is assessed as per this principle depending on the following factors: body mass index, lipid parameters values, criteria of metabolic syndrome diagnostics, blood pressure etc. [4, 8]. Such procedures for determining numeric risk assessment sometimes can't be easily applied in clinical practice due to complicated calculations required for their obtaining. Automated calculators which make this process much more simple as a rule allow to process data obtained via screening research and can't provide systemic assessment which allows for not only clinical parameters but also biochemical ones [5].

We set the following tasks within the framework of the present research:

¨ to work out efficient screening laboratory and diagnostic techniques for early detection of IHD risk factors based on biochemical parameters analysis;

¨ to apply logical and mathematical models for obtaining numeric values of the disease risk;

¨ to work out a user-friendly program module which would allow to assess IHD risk on the basis of biochemical parameters analysis.

Data and methods. We performed our research on 172 patients suffering from ischemic heart disease together with coronary atherosclerosis verified by coronary arteriography data; and on 167 patients without IHD according to the research data. Our research program included demographic and social data, questioning on tobacco and alcohol addiction, questioning

on dietary habits, chronic diseases case history, medications prescriptions history, cardiologic questioning as per Rose, anthropometry, triple blood pressure measuring, spirometry, and electrocardiogram taking with decoding as per Minnesota code. Biochemical parameters of each patient were also determined. Assessment of coronary atherosclerosis risk was performed with a logical and mathematical technique. Our logical and mathematical model was based on a laboratory and diagnostic complex which had been previously worked out in Scientific Research Institute for Therapy and Preventive Medicine. This complex included the most informative oxidative, lipid-lipoprotein, inflammatory, and metabolic biochemical parameters which characterized basic pathogenetic reasons for coronary atherosclerosis: initial level lipid peroxidation products in low density lipoproteins (LP0), low density lipoproteins resistance to oxidation (LP30), insulin concentration in blood (Insulin), C-reactive protein concentration (CRP), apoprotein A1 (apoA1) and B (apoB) concentration, triglycerides (TG) concentration, and cholesterol - high density lipoproteins concentration [2, 3, 17]. The model allowed for the weight of each parameter characterizing different contribution made into the overall diseases clinical picture, "standard - pathology" boundaries revealed for each parameter, and a standardization technique.

Algorithm of calculating IHD risk values for the obtained laboratory-clinical panel consists of three main stages. First, nxi interval values "standard - pathology" are set for each xi parameter. Second, a standardization technique is set for each xi depending on a measuring scale and value analysis logic. Third, α_i weighted average assessment of a contribution made by each parameter into the overall integral IHD risk

assessment is made via Delphi method. After that an integrated model is formed; it allows to calculate a uniform overall assessment allowing for contribution made by each xi standardized value by their "standard - pathology" interval values:

$$_n x_i : y = \sum_{i=1}^{8} \alpha_i f(x_i),$$

where α_i is a weighing coefficient which allows for a parameter contribution obtained via Delphi method;

$f(x_i)$ is a logical-mathematical function for recalculating an initial value of each of all 8 x parameters, allowing for the logic of initial parameter analysis and a way of its recalculation relative to nxi "standard - pathology" set by an expert for each xi, for .

To obtain the integrated model, we tested it on actual data and assessed it with calculating such characteristics as diagnostic accuracy, specificity, and sensitivity [12].

Sensitivity (Se) is a diagnostic technique capacity to give a correct result which is determined as a share of true positive results among all the conducted tests.

Specificity (Sp) is a diagnostic technique capacity not to give any false positive results in case there is no disease; it is determined as a share of true negative results among healthy people in the examined group.

Diagnostic accuracy (Ac) is a share of correct test results (i.e. sum of true positive and true negative results) among all the examined patients.

Results and discussion

The result of the conducted experiment (Figure 1) for the created model support on the total database on patients with diagnosed IHD (1) and without the diseases (0) allows to determine ranges of models threshold values which can be changed de-

pending on a task being performed (screening, prediction, etc.). Optimal threshold value for Ac-Sp-Se three parameters ratio is 0.6 when it concerns screening task or IHD risk assessment. This threshold coefficient allows to obtain calculated risk assessment values within 0 - 200 points range (standard reduced units of risk evidence); here 0-80 points range of IHD probability assessment means there is no IHD risk; 81-150 points range proves there is IHD risk; when a range lies beyond 150 points, it means IHD risk is very high.

Let us consider peculiarities of the created technique application on the example of three patients whose data are given in Table 1. To calculate risk assessment, we apply parameters values obtained on the logic of laboratory research results

analysis and techniques used for their recalculation relative to "standard - pathology" interval value set by an expert.
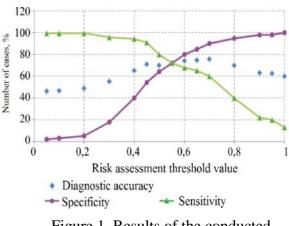

Figure 1. Results of the conducted experiment

Example of three patients

Parameters	Параметр								
	LP0	LP30	Insulin	CRP	apoA1	apoB	CS-HDL	TG	IDS
Initial values									
Patient A	0,5	31,7	6,8	2,21	186,99	83,69	70	105	0
Patient B	1,8	23,2	1,74	9,07	133,3	169,1	38	195	1
Patient C	1,3	24,1	3,46	4,98	132,7	93,87	70	59	0
Recalculated values									
Patient A	0,00	1,40	0,08	0,11	0,12	0,18	0,00	0,00	22
Patient B	0,20	0,43	0,00	1,10	1,30	1,50	1,20	1,40	171
Patient C	0,00	0,51	0,00	1,10	1,30	0,69	0,00	0,00	88

Values calculation algorithm allows to obtain assessment of deviations from conditionally permissible standard. As we interpreted results as per 8 considered parameters, we made all the initial scales and different "standard - pathology" boundaries ranges to look similar to achieve uniformity and convenient interpretation. It allowed us to assess how close this or that parameter was to a standard (close to 0). When IHD risk is assessed, all the recalculated values for each parameters are taken into account with their weighing coefficients obtained

via Delphi method. When results are visualized (Figure 2) one can see pathogenetic picture peculiarities which become apparent through deviations in s standardized parameter from a conditional "standard - pathology" boundary which is represented by a red line on the graph.

To make IHD risk assessment easier, a program module has been developed (state registration certificate for software No. 2017612582 dated March 01, 2017); it allows to get an assessment value with the use of the created logical and mathe-

matical model. This program module window is given in Figure 3; it is used for data input and risk assessment calculation. A user can input research data and press a "Calculate" button to get the result. On the basis of this result a physician can prescribe additional examinations if IHD risks for a patient are average or high.
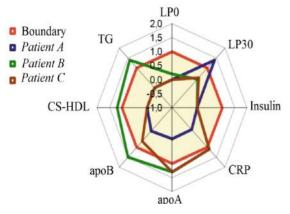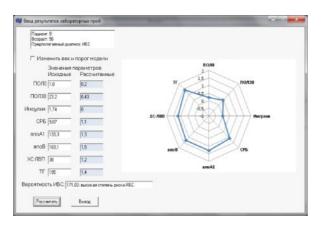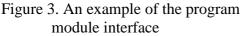

Figure 2. Visualization of the results obtained for three patients

Figure 3. An example of the program module interface

The obtained integrated model was tested with the use of actual data; diagnostic accuracy, specificity, and sensitivity were also calculated for all the examined patients. One of the testing results which illustrates the model verification is given in Figure 4.
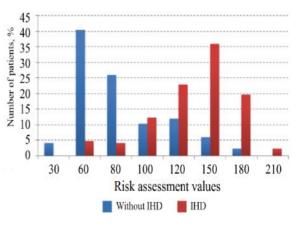

Figure 4. The result of assessing the model accuracy

Conclusions

So, we obtained the following results and came to the following conclusions in the course of our research:

Analysis of risk meters and scales which are widely used in cardiology allowed us to reveal that when risks were calculated, such assessments practically never included a set of oxidative, lipid-lipoprotein, inflammatory, and metabolic biochemical parameters.

Techniques aimed at obtaining numeric assessments as a rule require human processing of various parameters values and allow to form a set of assessments in different scales or one consolidated risk assessment.

As per results of the performed analysis we refined our task of creating techniques and models for IHD risk assessment on the basis of inflammatory, oxidative, and lipid biomarkers.

We developed a system of logical and mathematical models which is a universal scheme for laboratory parameters processing as it allows for heterogeneous data peculiarities. When we tested this developed model support, we obtained results which proved our models were highly accurate and their parameters gave a lot of

possibilities to increase specificity or sensitivity which are very important in screening or individual examinations of patients.

Our developed system of logical and mathematical models is universal, but diagnostic approach to applied biochemical parameters is specific.

The developed program module (calculator) allows a physician to obtain a result based on laboratory examinations data; this result characterizes numeric risk of coronary atherosclerosis and IHD for a patient. A physician can also see a visualization of a set of parameters on a screen and to detect their deviations from "standard - pathology" conditional boundary.

The developed laboratory-diagnostic complex is implemented into practical activities of the Scientific Research Institute for Therapy and Preventive Medicine.

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