

A Model for the Multifactorial Assessment of the Risk Index for the Progression of Coronary Heart Disease

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Abstract The development of a computer program for assessing the risk index for the development of an unfavorable course of coronary heart disease, depending on clinical and laboratory markers as well as modern cardiovisualizing diagnostic criteria of the progression of coronary atherosclerosis, is presented. The computer program is based on the results of logistic regression analysis of the most significant predictors of destabilization of coronary atherosclerosis detected by multispiral computer coronary angiography. A personalized approach to early diagnosis using an electronic predictive platform will reduce the frequency of manifestations of the disease. This circumstance dictates the need for practical application of the software product as new information and communication technologies in the healthcare system.

Keywords Coronary artery disease, Coronary atherosclerosis, Agatston coronary artery calcium score, Coronary computed tomography angiography, Computer program

1. Introduction

Cardiovascular diseases (CVD) are the most common cause of morbidity and mortality of the population and one of the most important medical, social and economic problems of modern society. According to World health organization (WHO), "...CVD and its complications are widespread among the adult population and are the leading cause of premature death and early disability in most economically developed countries of the world. More than 75% of CVD deaths occur in low- and middle-income countries. According to statistical studies, out of 17.9 million deaths from cardiovascular diseases, about 7 million people die annually from coronary heart disease (CHD)" [1].

To support such expansion of cardiovascular disease prevention and control efforts, WHO has developed tools and guidance, including risk prediction charts [2,3]. Risk prediction models can be a component of cardiovascular disease prevention and control efforts, because they can help to identify people at high risk of cardiovascular disease who should benefit the most from preventive interventions [4]. Many such risk prediction models have been developed [5,6], usually estimating individual risk over a 10-year period by use of measured levels of conventional risk factors for cardiovascular disease [2]. However, available models have limitations for use in low-income and middle-income countries. Most models were derived and validated with use of a narrow set of studies, might be directly applicable only to specific populations (mainly in high-income countries),

and might not predict the correct risk in the target population being screened (ie, poor calibration) [7,8].

On the basis of the prevention of CVD, and, in particular, coronary heart disease, lays the concept of correction of cardiovascular risk factors, the study and possibilities of exposure, on which a priority is given worldwide. At the same time, the currently accepted approaches to the individual prediction of cardiovascular diseases, based on the analysis of traditional risk factors (RF) and the calculation of the "total risk" by scales, are not always effective [9]. The results of a number of multicenter and domestic clinical studies dictate the need for a multifactorial pathogenetically based comprehensive assessment, so along with behavioral RF, to take into account the presence of psychosocial RF [10,11], the values of biochemical [12], hemobiological [13,14], immunochemical [15] markers for predicting the course of coronary heart disease. This justifies the need to develop highly sensitive and easy-to-use methods for predicting the risk of adverse cardiovascular events for timely identification of high-risk groups with subsequent decision of patient management tactics. To simplify and speed up the work of a doctor, it is advisable to collect and process information using computer programs [16], which allow automating the identification of the risk of destabilization of chronic diseases, followed by recommendations for the prevention of adverse cardiovascular outcomes. Medical information systems are becoming increasingly important on the way to digitalization of healthcare structures and optimization of processes within medical and preventive institutions [17]. The widespread use of information and communication technologies (ICT) in medical practice requires practitioners to have the skills and abilities to operate computer programs at the user level, as

well as the formed competence of doctors in the possession of professional information technologies. In order to provide cardiologists, internists and family doctors with programs for early diagnosis and tactics of CHD administration. Computer processing of information was directed to calculating the risk index for the progression of coronary atherosclerosis, depending on the presence and severity of key predictors of adverse outcomes of coronary artery disease. The objective of the developed medical technology is to increase the accuracy of predicting coronary heart disease by increasing the number of analyzed factors due to highly sensitive markers that have prognostic value for assessing the risk of coronary heart disease manifestation, which allows to effectively compile and analyze personalized data of cardiac patients.

2. Materials and Methods of Research

The objects of the clinical study were 152 patients with coronary heart disease, both genders, aged from 48 to 73 years. The main group included 73 patients with unstable angina pectoris (UAP). The comparison group consisted of 79 patients with stable angina pectoris (SAP) III FC.

At the initial stage of the study, all patients underwent a questionnaire (assessment of socio-anamnestic, behavioral, psychosocial RF and the degree of adherence to treatment), a comprehensive examination, including studies of clinical and functional status (ECG, EchoCG), biochemical (lipid spectrum, coagulogram), hemobiological (thromboprofile), immunochemical (analysis of biomarkers of inflammatory response) indicators of patients with coronary heart disease.

In the course of the study, a new medical technology was developed that allows assessing the risk of developing the progression of coronary heart disease with subsequent recommendations for further administration of cardiac patients, in the form of a computer program (CP) "Cardio Predict". CP is developed on the basis of the 1C: Enterprise software product version 8.3. and works in off-line mode.

To assess the effectiveness and prognostic significance of the developed CP, comparisons were made with the value of the calcium index determined using multispiral computed tomography (MSCT) of the coronary arteries, a non-invasive method for diagnosing the degree of coronary artery damage and destabilization of coronary sclerosis.

Statistical processing of the obtained results was carried out using Microsoft Excel spreadsheets and a package of statistical programs STATISTICA 6.0, SAS 6.3. An electronic database was created using Excel Microsoft Office 2012. On the basis of logistic regression models, odds ratios (OR) corresponding to 95% confidence interval (CI) and p-value (Wald criterion) were calculated. Spearman correlation analysis was used. The level of statistical significance was considered to be $p < 0.05$.

3. Results and Their Discussions

In the course of the study, a comparative assessment of the

basic characteristics, prevalence of RF and clinical and laboratory parameters of patients with coronary heart disease of both groups was carried out. The results of a comparative assessment of the occurrence of cardiovascular risk factors showed that smokers were 2 times more common among UAP patients in 31.3% of cases versus 14.8% in the comparison group ($p < 0.01$). Physical activity in patients with SAP was higher by 10.2%, relative to the main group, but was not of a reliable nature. The average body mass index (BMI) values did not differ in the main and compared groups, which amounted to 32.8 ± 1.14 and 30.1 ± 1.00 kg/m², respectively, but the degree of obesity in UAP patients tended to increase with a predominance of grade 3 by 2.6 times ($p < 0.01$) relative to the comparison group. When using psychometric research methods in patients with coronary heart disease, a frequent occurrence of psychosocial RF, in particular anxiety-depressive syndrome (ADS), was revealed in 41 (56.1%) of UAP patients, compared with 34 (43%) of SAP patients.

A comparative analysis of clinical, functional, and biochemical parameters revealed that UAP patients experienced a more severe clinical course. This was characterized by a 20% increase in hypertension ($p < 0.01$) primarily due to elevated systolic blood pressure (SBP) by 8% ($p > 0.05$), a higher level of pain intensity by 12% ($p < 0.05$) according to a Visual analog scale (VAS), a longer duration of anginal pain ($p < 0.01$), and a higher frequency of angina attacks ($p < 0.05$), and destabilization of blood pressure ($p < 0.05$), as well as lower exercise tolerance (ET) ($p < 0.05$) and increased sizes of interventricular septal thickness (IST) and left ventricular posterior wall thickness (LVPWT) ($p < 0.01$). Also, UAP patients had significantly higher indices of total cholesterol (TC) ($p < 0.01$), LDL-C and atherogenic coefficient (AC) ($p < 0.001$), elevated values of fibrinogen ($p < 0.001$), prothrombin index (PTI) ($p < 0.01$) and low indicators of prothrombin time (PT), thrombin time (TT) and activated partial thromboplastin time (APTT) ($p < 0.01$), which indicates a more severe clinical course of CAD caused by anxiety-depressive syndrome. According to the hemobiological indicators in UAP patients, the risk of developing shifts in the morphological picture of platelets increased by 2.3 and 2.5 times, which indicates a high thrombogenic risk of blood due to destabilization of coronary sclerosis.

In patients with UAP, there was a significant predominance of the average values of key cytokines, such as interleukin-6 (IL-6) by 2.1 times and TNF- α by 2.6 times in relation to these indicators of patients in the comparison group, respectively ($p < 0.05$). This fact indicates the predisposition of patients with coronary heart disease to the progression of the disease with increased production of inflammatory markers, through cardiac depression.

When processing the data of CHD patients during the questionnaire, the total score of the degree of adherence to the main therapy was calculated, which was $40.5 \pm 4.29\%$ in the main group, which corresponded to a very low level of compliance of UAP patients. Whereas, in the comparison group, the degree of adherence to therapy was significantly

higher and amounted to $68.7 \pm 3.76\%$ in patients with CHD ($p < 0.01$).

In order to assess the predictor value of the dominant factors having independent pathogenetic significance in the processes of atherogenesis, the interrelated influence of which leads to the progression of coronary heart disease, a multifactorial logistic regression analysis was carried out.

Based on the regression analysis, the most significant independent predictors of the destabilization of the CHD course were identified, in descending order by degree of significance, they turned out to be: the combination of an increased concentration of IL-6/TNF- α and low adherence to treatment - OR 8.92, CI 2.01-38.43 ($p = 0.003$), elevated levels of IL-6 and/or TNF in the blood - OR 1.87, CI 1.34-2.78 ($p = 0.001$), non-adherence to pharmacotherapy - OR 1.72, CI 1.14-2.89 ($p = 0.015$), combined anxiety-depressive states - OR 2.27, CI 1.08-4.82 ($p = 0.038$), dyslipidemia - OR 2.31, CI 1.54-3.47 ($p = 0.001$), Systolic blood pressure per 20 mm Hg - OR 1.75, CI 1.08-2.85 ($p = 0.028$), obesity - OR 1.53, CI 0.96-2.37 ($p = 0.05$), smoking - OR 1.55, CI 0.88-2.72 ($p = 0.05$), male sex - OR 2.05, CI 0.91-4.39 ($p = 0.05$) and age > 60 - OR 3.78, CI 1.11-13.14 ($p = 0.035$).

The multifactorial nature of the development and progression of major CVD requiring timely comprehensive assessment, the heterogeneity of patient groups in real outpatient practice, the lack of a sufficient number of methodological programs in the system of early diagnosis of destabilization of coronary heart disease encourages us to look for new ways to organize a system for assessing and predicting adverse cardiovascular events in conditions of long-term outpatient follow-up.

To implement this direction, an electronic platform has been developed, in the form of a computer program (CP) "Cardio Predict". To build a computer model for assessing the risk index for the progression of coronary heart disease, we took indicators with established predictor significance, most of which data are almost always present in the outpatient chart: these are the gender and age of the patient, the degree of hypertension, the presence of psychosocial and behavioral RF: ADS, smoking, obesity and compliance with the doctor's recommendations.

Multivariate regression analysis showed that all significant predictors of the progression of coronary heart disease have almost the same weight in determining the risk of adverse angina. Optimally, the doctor at the reception, when determining the chance of developing unstable angina in a patient with CHD, needs to calculate the contribution of each significant factor, since each factor has its own weight. However, with the tight time frame in which the doctor is assigned on an outpatient appointment, it is quite difficult to calculate the contribution of each factor to identifying the risk of progression of coronary heart disease. During the study, the numbers of predictor factors contributing to the manifestation of the clinical condition of CHD patients were summarized, namely: in the presence of 1 of any factor, the chance of CHD progression increases 2.9 times, in the presence of 2 of any factors, the chance of CHD progression increases 3.2 times, any three factors increase the chance of

CHD progression times, 4 factors – they increase the chance of CHD progression by 9 times, the presence of 5 factors increases the chance of CHD progression by 16.5 times (the frequency of UAP development exceeds 80%).

The data obtained during the study are taken as the basis of the developed combined digital model for quantifying the risk of an unfavorable course of coronary heart disease in the form of a computer program that takes into account the personal data of patients, subtracting the prognostic integral index of the probability of developing UAP with subsequent suggested recommendations for the complex administration of cardiac patients.

A feature developed by the CP is the ability to provide a printed version of the data of the assessment of the risk index for the development of adverse events of CVD, as well as recommendations for each patient, which can be embedded in an outpatient chart and periodically monitor the dynamics of the condition of patients with coronary heart disease. The information of the analysis of the compliance assessment data of the patient who applied to the practitioner and the recommendations issued at the time of the visit are stored in the database.

In order to assess the diagnostic and prognostic effectiveness of the practical application of CP, 42 outpatient patients with CHF were monitored by the noninvasive method of multispiral computed tomography (MSCT) coronary angiography for screening coronary artery lesions, with an assessment of the calcium index (CI). American researchers led by Arthur Agatston developed a method for assessing the amount of coronary artery calcium using CT [18]. They found that the presence and degree of coronary calcium are a marker of the degree of atherosclerosis in the coronary arteries. Both the degree of calcification and the patterns of its distribution are of prognostic importance, however, the relationship of calcification of the coronary arteries with the instability of atherosclerotic plaque is extremely complex and has not been fully studied.

MSCT angiography of coronary arteries is a sensitive method for detecting coronary artery disease (sensitivity 95-99%) and allows detecting small arterial stenoses. At the same time, the widespread use of the method is limited by its high cost, the impossibility of using contrast iodine-containing substances in patients with an allergy to iodine and with severe damage to kidney function [19]. Analysis of the degree of risk of an unfavorable course of CHD with the use of CP showed that in 8.4% of cases the chance of progression increases 2.9 times, in 7.9% of patients 3.2 times, in 17.3% 5.6 times, in 26.8% 9 times, as well as in most patients in 39.6% of cases the chance of developing UAP increases 16.5 times.

In order to assess the prognostic value of the probability index of the progression of coronary artery disease issued by CP, a correlation analysis was performed with the indicators of MSCT angiography, which revealed a significantly high positive relationship between the level of coronary calcium coefficient and the chance of developing UAP ($r = 0.75$; $p < 0.001$), which indicates a significant associative relationship of the degree of calcification of the coronary arteries with an

increased index of unstable flow CHD. It is noteworthy that CI showed a high correlation with the number of stenoses ($r=0.876$, $p<0.001$) and the maximum degree of stenosis ($r=0.896$, $p<0.001$). The average relationship was observed with the presence of angina pectoris ($r=0.518$, $p=0.002$) and the functional class of angina pectoris ($r=0.541$, $p=0.001$), weak – with the age of patients ($r=0.452$, $p<0.05$).

The results obtained prove the safety and high efficiency of the use of digital methods for predicting the risk of adverse cardiovascular events in patients with coronary heart disease, by quantifying a number of clinical and laboratory indicators. The prognostic role of clinical and laboratory markers and cardiovascular risk factors with the obtained evidence of the predictive significance of the state of coronary sclerosis allows not only to improve the stratification of the risk of an unfavorable course of coronary artery disease, but also to identify a high-risk group of UAP for dispensary observation, assessing the personal risk of progression of coronary artery disease at an early stage of the manifestation of the disease, which leads to timely correction of treatment tactics and reduction of the risk of exceptionally high premature mortality in this severe cohort of patients. Ultimately, this makes it possible to reduce the economic costs of prevention and treatment of socially significant cardiovascular pathology.

4. Conclusions

Thus, in order to achieve high efficiency of early diagnosis of the progression of coronary heart disease in the process of secondary prevention in routine outpatient settings, it is necessary to use information and communication technologies in the practice of a doctor. However, the possibility of using electronic-technical platforms for diagnostics and forecasting is still closely related to the material and technical base of the departments. Proper technical provision of outpatient and inpatient facilities and the activity of practitioners regarding the use of information technologies make it possible to timely prevent adverse outcomes of CVD and personalized effects on a cardiological patient, increase the effectiveness of professional medical activities; reduce time in the process of calculations, statistical processing of analysis results; activation and large-scale implementation of digitalization in healthcare.

The introduction of the developed new medical technology - Method for predicting the risk of adverse cardiovascular events in patients with ischemic heart disease, allows for an objective assessment of the severity of the disease and determine the risk of adverse cardiovascular events, which will lead to a reduction in the duration of hospitalization and, ultimately, as a result, it will reduce the costs of the state for the treatment and prevention of socially significant pathology.

REFERENCES

- [1] «WHO report on the situation in the field of cardiovascular diseases in the world 2016» Panev N.I., Filimonov S.N., Korotenko O.Yu., Panev R.N., Paneva N.Ya. Elaboration of new medical technology for predicting the risk of ischemic heart disease in the workers of the coal industry. *Acta biomedica scientifica*. 2019; —№ 4(3): 52-57. doi: 10.29413/ABS.2019-4.3.7.
- [2] World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions Author: Stephen Kaptoge, Lisa Pennells, Dirk De Bacquer, Marie Therese Cooney, Maryam Kavousi, Gretchen Stevens, Leanne Margaret Riley, Stefan Savin, Taskeen Khan, Servet Altay, Philippe Amouyel, Gerd Assmann, Steven Bell, Yoav Ben-Shlomo, Lisa Berkman, Joline W Beulens et al. Publication: The Lancet Global Health Publisher: Elsevier Date: October 2019.
- [3] WHO Package of essential noncommunicable disease interventions in primary health care. https://www.who.int/ncds/management/pen_tools/en/ Date accessed: July 26, 2019.
- [4] Karmali KN Persell SD Perel P Lloyd-Jones DM Berendsen MA Huffman MD Risk scoring for the primary prevention of cardiovascular disease // *Cochrane Database Syst Rev*. 2017; 3CD006887.
- [5] Piepoli MF Hoes AW Agewall S et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the sixth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention and Rehabilitation (EACPR) // *Eur Heart J*. 2016.—№ 37: 2315-2381.
- [6] Pylypchuk R Wells S Kerr A et al. Cardiovascular disease risk prediction equations in 400 000 primary care patients in New Zealand: a derivation and validation study // *Lancet*. 2018.—№ 391: 1897-1907.
- [7] Ueda P Woodward M Lu Y et al. Laboratory-based and office-based risk scores and charts to predict 10-year risk of cardiovascular disease in 182 countries: a pooled analysis of prospective cohorts and health surveys // *Lancet Diabetes Endocrinol*. 2017. —№ 5: 196-213.
- [8] Mortensen MB Nordestgaard BG Comparison of five major guidelines for statin use in primary prevention in a contemporary general population // *Ann Intern Med*. 2018; —№ 168: 85-92.
- [9] Bernstein LL, Katamadze NO, Laznam SS, Grishkin YuN. Individual coronary heart disease risk prediction as part of primary prevention // *Kardiologiya*. 2012. —№ 52(10): 65-74.
- [10] Albus, C., Waller, C., Fritzsche, K. et al. Significance of psychosocial factors in cardiology: update 2018 // *Clin Res Cardiol* 2019—№ 108, 1175–1196. <https://doi.org/10.1007/s00392-019-01488-w>.
- [11] Abdumalikova F.B. Analysis of the level of compliance with pharmacotherapy in patients with chronic diseases depending on the psychological and typological properties of the CNS // *Infection, Immunity and Pharmacology*. - Tashkent, 2017. - No. 2. - P. 11-17.

- [12] Thupakula, S., Nimmala, S.S.R., Ravula, H. et al. Emerging biomarkers for the detection of cardiovascular diseases // *Egypt Heart J* 2022.—№ 74, 77. <https://doi.org/10.1186/s43044-022-00317-2>.
- [13] Huseynov, A.; Reinhardt, J.; Chandra, L.; Dürschmied, D.; Langer, H.F. Novel Aspects Targeting Platelets in Atherosclerotic Cardiovascular Disease—A Translational Perspective // *Int. J. Mol. Sci.* 2023. — № 24, 6280. <https://doi.org/10.3390/ijms24076280>.
- [14] Abdumalikova F.B., Nurillayeva N.M. Influence of psychological and personality characteristics of patients with coronary artery disease on the phenotype of platelets // *European journal of pharmaceutical and medical research.* 2019. - № 6(5). —P. 662-666.
- [15] Subirana, I., Fitó, M., Diaz, O. et al. Prediction of coronary disease incidence by biomarkers of inflammation, oxidation, and metabolism // *Sci Rep* 2018. — № 8, 3191. <https://doi.org/10.1038/s41598-018-21482-y>.
- [16] Gomez E. A., Katia P. Information and communication technologies (ICT) options for local and global communities in health-related crisis management // *J Commun Informat.* 2010. — № 6.
- [17] Monakov D.M., Altunin D.V. Medical information systems: modern realities and prospects // *Russian Journal of Telemedicine and E-Health* 2022; 8(4): 46-53; <https://doi.org/10.29188/2712-9217-2022-8-4-46-53>.
- [18] Noortje van der Bijl, Raoul M. S. Joemai, Jacob Geleijns, Jeroen J. Bax, Joanne D. Schuijf, Albert de Roos, and Lucia J. M. Kroft. Assessment of Agatston Coronary Artery Calcium Score Using Contrast-Enhanced CT Coronary Angiography // *American Journal of Roentgenology.* 2010. Vol. 195. —№ 6. <https://doi.org/10.2214/AJR.09.3734>.
- [19] Danad I., Raijmakers P.G., Driessen R.S. et al. Comparison of Coronary CT Angiography, SPECT, PET, and Hybrid Imaging for Diagnosis of Ischemic Heart Disease Determined by Fractional Flow Reserve // *JAMA Cardiol.* 2017. – Vol. 2, № 10. – P. 1100–1107.
- [20] Abdumalikova FB, Nurillaeva NM. Crucial aspects of noninvasive methods of cardiovascular visualization in the early diagnosis and prognosis of coronary artery diseases. *European Journal of Pharmaceutical and Medical Research.* 2023; 10 (12), – P. 54-58.