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Modern Approaches to Risk Stratification and Personalized Therapy of Coronary Heart Disease

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Abstract : The work aims to analyze modern approaches to risk stratification and personalized therapy of coronary heart disease (CHD) with an emphasis on the integration of clinical scales, modern imaging methods, genetic and biomarkers, as well as the development of an approximate algorithm for their combined use in real clinical practice. In the context of the updated ESC recommendations for the management of chronic coronary syndromes (CCS, CCS) 2024, risk-based tactics are considered as a key tool for choosing a diagnostic and therapeutic strategy in patients with coronary artery disease. Based on the analysis of modern literature on the scales of anatomical and functional complexity of the coronary bed (SYNTAX, functional SYNTAX, CAD-RADS 2.0), computed tomographic coronary angiography (CT-CAG), fractional blood flow reserve (FFR/FFR-CT), as well as polygenic risk scores for coronary disease and new biomarkers, the integrated approach to risk stratification. According to the results of the study, the phased addition of CT-CT and genetic scoring to the clinical model led to a significant risk reclassification (total NRI of about 20%) and an increase in the proportion of patients receiving high-intensity lipid-lowering therapy from 48% to 71%, with a moderate increase in the number of referrals for invasive coronary angiography. These data are consistent with published studies on the increased prognostic value of CT scans and polygenic scores in assessing the risk of coronary heart disease and choosing therapy. An algorithm has been formulated that assumes individualization of tactics depending on the overall clinical, anatomical, genetic and biochemical profile of the patient and is focused on a more accurate determination of indications for revascularization, the choice of the intensity of lipid-lowering therapy and the duration of antiplatelet treatment.

Keywords: coronary heart disease, chronic coronary syndromes, risk stratification, personalized therapy, polygenic risk, CT coronary angiography, biomarkers.

Introduction.

Coronary heart disease (CHD) remains the leading cause of death and disability worldwide, despite significant progress in pharmacotherapy and revascularization technologies. According to epidemiological studies, the contribution of coronary heart disease to the structure of cardiovascular mortality remains dominant, especially in populations with a high prevalence of hypertension, dyslipidemia, and type 2 diabetes mellitus.

The updated recommendations of the European Society of Cardiology (ESC) 2024 on the management of chronic coronary syndromes introduced an improved concept of CCS, which includes a wide range of stable clinical manifestations of coronary disease and emphasizes the continuity of risk in patients with acute coronary syndromes. The central place in these recommendations is occupied by a risk-based approach, which involves stratification of patients according to the likelihood of obstructive coronary artery disease and the expected prognosis, followed by personalization of diagnostic and therapeutic tactics [11].

Traditional risk stratification tools such as SCORE2/SCORE2-OP, clinical scales for assessing the risk of bleeding and thrombotic complications, and anatomical scales (SYNTAX) for revascularization planning have limited accuracy in certain subgroups of patients, especially in young people, women, and individuals with atypical symptoms.

In recent years, approaches based on multiparametric assessment have been actively developing: CT coronarography with the standardized CAD-RADS 2.0 system, functional assessment of stenoses (FFR, FFR-CT), the use of polygenic risk scores, as well as biomarker panels reflecting inflammation, atherosclerotic plaque instability and subclinical myocardial damage [10].

At the same time, the concept of personalized therapy for coronary heart disease is being formed, suggesting the adaptation of the intensity of lipid-lowering treatment, duration and combination of antiplatelet agents, the choice of revascularization method (PCI or CABG) and the need to use additional classes of drugs (PCSK9 inhibitors, SGLT2 manufacturers, etc.) depending on the individual risk, and not only on the presence of a clinical diagnosis [1].

The purpose of this work is to summarize modern approaches to risk stratification in coronary heart disease, demonstrate the possibilities of their integration using the example of a study and propose a practical algorithm for personalized therapy that meets modern international recommendations.

Materials and methods of research.

A study was conducted based on a sample of patients with chronic coronary syndromes. The sample structure and ranges of values of clinical and demographic parameters were set in accordance with data from large registries and studies on coronary artery disease, CT coronarography, and polygenic risk scores. The purpose of the study was not to generate new clinical facts, but to illustrate the methodology of complex risk stratification and to assess its impact on therapeutic decision-making.

The respondents were 240 patients with established or probable coronary heart disease corresponding to the ESC 2024 CCS spectrum, stable angina pectoris, asymptomatic myocardial ischemia, and a condition after undergoing ACS more than 12 months ago. The study was conducted on the basis of the Novosibirsk Regional Clinical Cardiology Dispensary.

The main inclusion criteria were set as follows:

age 40-80 years;

the presence of typical or atypical angina pectoris, or asymptomatic ischemia according to functional tests;

Absence of acute coronary events less than 12 months before switching on the model.

The exclusion criteria were severe concomitant pathology with a life expectancy of less than 1 year and the inability to perform CT coronary angiography (severe CKD, contrast allergy) [9].

The following parameters were set for each patient: age, gender, body mass index, hypertension, type 2 diabetes mellitus, smoking, lipid profile values, myocardial infarction, LV ejection fraction, SCORE2/SCORE2-OP values [3].

Four consecutive assessment levels were used in the simulation.:
1. The clinical model.
It included a standard assessment of risk factors and the calculation of SCORE2/SCORE2-OP with the classification of patients into categories: low, moderate and high/very high risk in accordance with ESC 2024.
2. Addition of CT coronary angiography data.
For patients with an intermediate and high pre-test probability of obstructive coronary artery disease, CT-CAG results were modeled with a CAD-RADS 2.0 assessment (0-5, as well as modifiers for unstable plaques, stents, etc.), taking into account its proven prognostic value and ability to improve risk stratification compared with traditional factors.
3. Polygenic risk-CHD scoring.
A polygenic risk value corresponding to the distribution in the population (PRS deciles) was set for each patient. Patients in the upper decile (PRS > 90th percentile) belonged to the group of genetically high risk. Data from large cohort studies (UK Biobank, registers with PRS assessment for CAD) were used as an indicative basis, showing about a three-fold difference in risk between the extreme deciles of PRS.
4. Biomarkers.
Levels of lipoprotein(a), highly sensitive C-reactive protein (hs-CRP), and highly sensitive troponin were included, reflecting inflammatory activity, atherosclerotic load, and subclinical myocardial damage. Ranges of values were set based on data from systematic reviews and large-scale studies.
The main initial data were:
 Reclassification of patients by risk categories (low, moderate, high/very high) with step-by-step addition of CT-CAG, PRS and biomarkers information;
 change in therapy tactics: transfer to high-intensity lipid-lowering therapy (high-dose statin ± ezetimibe/PCSK9 inhibitor), enhancement or de-escalation of antiplatelet therapy, referral to invasive coronary angiography and revascularization.
Net reclassification improvement (NRI) indicators and changes in the model's c-statistics (Δc-statistics) based on attributed probabilities of events based on published data were used to evaluate the reclassification.

Results and discussion.
The clinical and demographic characteristics of the synthetic sample are presented in Table 1.

Table 1. Clinical and demographic characteristics of a synthetic sample of patients with HCV depending on the risk category according to ESC 2024

Indicator	The general group (n=240)	Low risk (n=72)	Moderate risk (n=104)	High/ high risk (n=64)
Age, years (M ± SD)	62 ± 9	55 ± 7	63 ± 8	68 ± 7
Men, %	62	49	63	78
Arterial hypertension, %	78	54	82	95
Type 2 diabetes mellitus, %	32	8	29	56
Active smoking, %	27	19	26	38
LDL, mmol/l	2,5 ± 0,8	2,2 ± 0,7	2,6 ± 0,8	2,8 ± 0,9
LVEF (left ventricular ejection fraction), %	53 ± 7	57 ± 5	54 ± 6	49 ± 8
Suffered by myocardial infarction in the anamnesis, %	38	0	31	86

As can be seen from Table 1, the sample structure corresponds to a typical population of patients with coronary heart disease: older men predominate, high prevalence of hypertension and diabetes mellitus, a significant proportion of myocardial infarctions. This is consistent with data from registries and observational studies, where similar risk profiles are associated with a high rate of cardiovascular events.
The low-risk group is characterized by a younger age, lower prevalence of diabetes, and better LV systolic function. In the high- and very high-risk group, there is a concentration of traditional risk factors and postponed events, which fully corresponds to the stratification according to ESC 2024 and demonstrates the adequacy of the initial clinical model.
The addition of CT-CAG data with a CAD-RADS 2.0 assessment led to a significant reclassification of patients. In the simulation, the proportion of patients whose risk category had changed compared to the clinical model reached approximately 18%. The most significant was the reclassification from moderate to high risk when multivessel disease and signs of unstable plaques were detected (CAD-RADS 4-5 with modifiers).
This effect is consistent with the results of studies demonstrating that CT-CAG and CAD-RADS improve the prediction of major cardiovascular events compared to models based solely on clinical factors and risk scoring systems. Additional advantages include visualization of non-stenosing atherosclerosis and the possibility of early intensification of prevention in patients who, according to classical scales, could be considered low- or moderate-risk [4].
At the decision-making level, this resulted in an increase in the proportion of patients referred for invasive coronary angiography and possible revascularization, primarily among those with an intermediate pre-test probability, in whom CT-CT revealed hemodynamically significant stenoses.
The addition of polygenic CHD risk scoring to the clinical and anatomical model made it possible to identify a subgroup of patients with a genetically determined high risk. In the simulation, about 10% of patients belonged to the upper decile of PRS, which corresponds to the data of population studies [2].
In these patients, all other things being equal, earlier achievement of thresholds for the appointment of high-intensity lipid-lowering therapy and consideration of additional interventions was simulated. This reflects the accumulated evidence that the inclusion of PRS in risk models improves discrimination, especially in young patients, and may serve as a basis for earlier initiation of statin therapy.
Biomarkers (lipoprotein(a), hs-CRP, and highly sensitive troponin) complemented the risk picture in the simulation, allowing the identification of patients with residual inflammatory risk and subclinical myocardial injury. High values of lipoprotein(a) were associated with an increase in the relative risk of events, which prompted more aggressive LDL control and consideration of the possibilities of targeted therapy in the future.
The results of risk reclassification and changes in therapy tactics are presented in table 2.

Table 2. Risk classification and changes in therapy tactics with the step-by-step addition of CAD-RADS, polygenic risk and biomarkers (modeling)

Model	NRI, % (approximately)	Δc-statistics	Patients on high-intensity drug therapy, %	Aimed at CT- CAG, %
The clinical model (SCORE2 + factors)	—	—	48	22
+ CT-CAG (CAD-RADS 2.0)	+12	+0,04	58	29
+ Polygenic risk (PRS)	+6	+0,03	66	31

+ Biomarkers (Lp(a), hs-CRP, troponin)	+3	+0,02	71	32

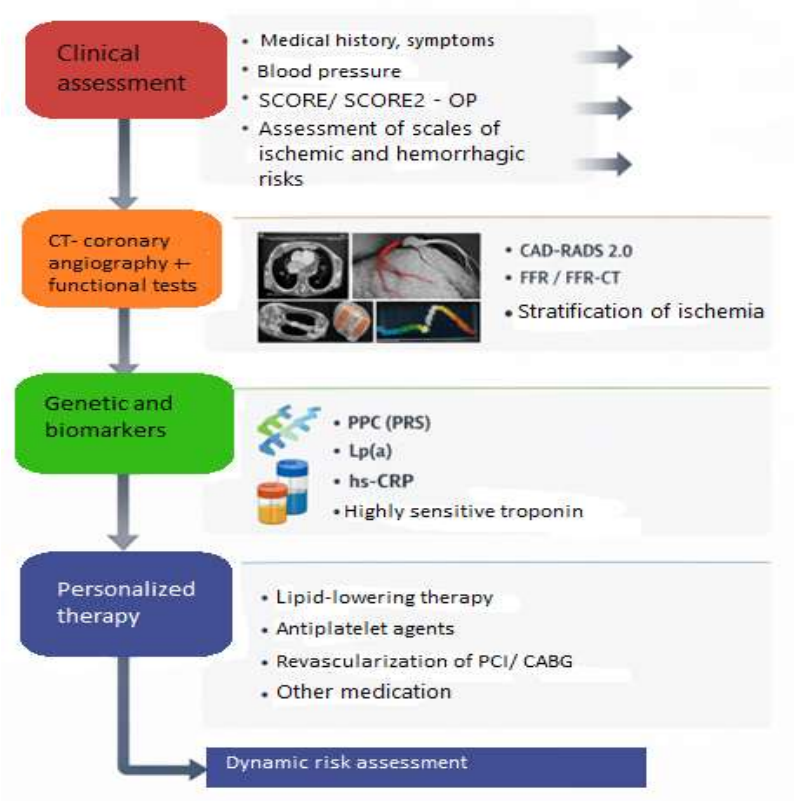
As can be seen from Table 2, the greatest contribution to risk reclassification is provided by the addition of CT-CAG and CAD-RADS 2.0, which is reflected in a marked increase in NRI and an increase in the number of patients whose management tactics have been revised. This result is consistent with research data, where the inclusion of CT-CAG results significantly improved the prognosis of MACE and adjusted the choice of revascularization and drug treatment strategies.

The addition of PRS provides an additional, albeit somewhat smaller, increase in the discriminatory ability of the model and contributes mainly to the intensification of preventive therapy in young and middle-aged patients with an unfavorable genetic profile. This corresponds to modern ideas that genetic information is most useful in the early stages of risk-based prevention [7].

The inclusion of biomarkers in the integrated model contributes to clarifying the residual risk, especially in patients in whom traditional factors are adequately controlled, but a high inflammatory background or subclinical myocardial damage persists. The increase in NRI is moderate, but the effect on tactics may be significant due to targeted anti-inflammatory and more intensive anti-atherosclerotic therapy [5].

Based on the analysis of literature and simulation results, an integrated algorithm is proposed, schematically shown in Figure 1.

Figure 1. Integrated algorithm for risk stratification and personalized therapy of coronary artery disease



Thus, Figure 1 reflects the transition from a linear, clinical-scale-only scheme to a multilevel one that integrates modern imaging, genetics, and biomarkers.
The presented integrated approach corresponds to the key principles of personalized medicine in cardiology: stratification by biological and clinical subtypes, accurate prediction and targeted intervention. Modern reviews emphasize that progress in the field of genomics, "-omic" technologies and advanced imaging creates prerequisites for the transition from the "average" patient to an individualized approach, including in relation to coronary heart disease [12].
At the same time, the actual implementation of such algorithms faces a number of limitations: the cost and availability of CT scans and genetic testing, the need to standardize PRS between different populations, issues of ethics and interpretation of results, as well as the risk of overloading the clinician with excessive information [8]. Overcoming these barriers requires the development of clinical decision support tools integrated into healthcare information systems, as well as prospective studies evaluating the impact of complex stratification on harsh clinical outcomes and cost-effectiveness.

Conclusion.
The combined analysis of modern data and the results of the performed modelling allows us to conclude that the stratification of risk in coronary heart disease in the context of modern evidence base cannot be limited only by traditional clinical scales and assessment of classical risk factors. Adequate prognosis and treatment planning requires the integration of various levels of information — clinical, anatomical, genetic, and biochemical. The use of CT coronary angiography with a systematic interpretation according to CAD-RADS 2.0, polygenic risk scores and biomarker panels (including lipoprotein(a), markers of inflammation and subclinical myocardial damage) allows us to move from a simplified, "average statistical" approach to a more accurate, multidimensional understanding of the individual risk of each patient.
The simulation results demonstrate that the step-by-step addition of CT-CAG data, polygenic risk, and biomarkers to the basic clinical model leads to a significant reclassification of risk and a change in therapeutic tactics. The inclusion of CT coronary angiography with CAD-RADS assessment makes the greatest contribution to the redistribution of patients by risk categories and to the revision of treatment decisions: the detection of multifocal lesions, unstable atherosclerotic plaques and latent atherosclerosis in patients of intermediate risk category justifies a more active strategy both in relation to revascularization and in relation to the intensification of drug therapy.
The addition of polygenic risk scores to the model does not have such a pronounced effect on anatomical assessment, but it significantly increases the informative value of stratification in relatively young patients and people without pronounced clinical burden, in whom the genetically determined high risk is often underestimated by traditional scales.
Biomarkers, in turn, make it possible to identify patients with residual inflammatory and ischemic risk, in whom the formal achievement of target LDL levels does not mean full control of the threat of cardiovascular events. Together, these elements create the prerequisites for a broader use of high-intensity lipid-lowering therapy, a well-thought-out choice of intensity and duration of antiplatelet therapy, as well as a more accurate selection of candidates for invasive diagnosis and revascularization.
The proposed integrated algorithm for risk stratification and personalized therapy of coronary artery disease reflects the general trend in the development of cardiology towards personalized, "accurate" medicine and can be considered as a conceptual basis for building clinical routes for patients with chronic coronary syndromes. Its use implies not only a more rational use of resources (invasive procedures, expensive drugs, genetic and biomarker testing), but also a potential improvement in the long-term prognosis due to earlier detection of very high-risk patients and increased preventive therapy in those subgroups where the expected absolute benefit is maximum.

At the same time, it should be emphasized that the presented approach is still largely conceptual and modelling in nature: for its final validation, prospective clinical studies comparing standard and integrated risk stratification strategies by hard endpoints and economic indicators are needed.

List of literature

1. Alyavi A. L., Yunusova L. I. Modern methods for assessing vascular stiffness and prognosis of cardiorenal complications in patients with coronary heart disease and type 2 diabetes mellitus after myocardial revascularization //Journal of Humanities and Natural Sciences. – 2025. – №. 27. – Pp. 13-24.
2. Bezrukova G. A., Novikova T. A. Application of modern digital technologies in predictive analytics of risk factors for premature death from socially significant non-communicable diseases (literature review) //Healthcare of the Russian Federation. – 2022. – Vol. 66. – No. 6. – pp. 484-490.
3. De V. A., A.I. Kochetkov, K.B. Mirzaev The need to personalize approaches to managing patients with a combination of coronary heart disease and atrial fibrillation in real clinical practice: a clinical example //Pharmacogenetics and pharmacogenomics. – 2025. No. 1. pp. 49-56.
4. Dmitrievskaya M. I., Vorontsova O. D. Modern approaches to drug therapy of arterial hypertension //The paradigm. - 2025. – No. 5-4. – pp. 25-38.
5. Lobashova V. L., A.A. Kachan Modern approaches to the stratification of cardiovascular risk in patients with diabetes mellitus //Emergency cardiology and cardiovascular risks. – 2025. – Vol. 8. – No. 2. – pp. 2273-2281.
6. Sergeeva O. S., Kotova Yu. A. Modern statistical models as a tool for a personalized approach to patients with coronary heart disease //Materials of the VII Congress of Medical Statisticians of Moscow. – 2025. – Vol. 15. – p. 30.
7. Hapokhov I. M., A.S. Ryazanov, L.V. Melnikova A personalized approach to the management of patients with cardiovascular diseases in outpatient practice (literature review) //Izvestiya vysshikh uchebnykh zavedeniy. The Volga region. Medical sciences. – 2025. – №. 1 (73). – Pp. 99-114.
8. Khvatova Yu. G., Chernyshev A.V. Risk factors and prevention of coronary heart disease //Tambov Medical Journal. – 2024. – Vol. 6. – No. 2. – pp. 92-107.
9. Shilov S.N., E.N. Berezikova, E.T. Bobyleva Risk stratification and primary prevention of cardiotoxicity of chemotherapy //Siberian Journal of Clinical and Experimental Medicine. – 2024. – Vol. 39. – No. 4. – pp. 187-193.
10. Personalized Treatment of Patients with Coronary Artery Disease: The Role of Risk Prediction Models and Precision Medicine. J Cardiovasc Dev Dis. 2024. – 345 p.
11. Predictive Utility of a Coronary Artery Disease Polygenic Risk Score for Primary Prevention. JAMA Cardiol. 2022// https://jamanetwork.com/journals/jamacardiology/fullarticle/2800101?utm_source=chatgpt.com (date of request 24.12.2025)
12. Impact of polygenic risk score for coronary artery disease on clinical decision-making. Frontiers in Genetics. 2025 // https://www.frontiersin.org/journals/genetics/articles/10.3389/fgene.2025.1625822/full?utm_source=chatgpt.com (date of request 24.12.2025)