MEDICAL SCIENCES

NATIONAL RUSSIAN CALCULATOR OF STRATIFICATION OF TOTAL RISK OF CARDIOVASCULAR COMPLICATIONS AFTER ACUTE MYOCARDIAL INFARCTION

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Abstract

In the State Budgetary Institution of Public Health of the Novosibirsk Region (Russian Federation) "Clinical City Hospital No. 1" (Regional Vascular Center), a calculator for stratification of the total risk of cardiovascular complications after acute myocardial infarction was invented. In a recent open Non-Randomized Parallel Group Study, an approach has been developed for determining the annual prognosis of a patient with myocardial infarction. The calculation of "personal coefficients of risk factors" allows assessing the significance of each factor in a particular patient, personifying rehabilitation and secondary prevention. This innovative approach solves the problem of low reproducibility of numerous prognostic risk scales TIMI, GRACE, PURSUIT, CADILLAC, RECORD. A significant drawback and the reason for the low information content of many assessment methods is that they were developed on the basis of the European and American populations without taking into account the specific factors of the countries of Eastern Europe, the CIS and the Russian Federation that affect the prognosis of patients with ACS.

Keywords: calculator; stratification of total risk of cardiovascular complications; acute myocardial infarction.

Description

The study included 1,000 patients admitted with STEMI in the Department of Myocardial Infarction at the Regional Vascular Center within the period from November 2017 to September 2018. In which 724 (72.4%) were male and 276 (27.6%) were female with an average age (57.5 ± 9.5) years. The diagnosis of acute myocardial infarction was established by a set of criteria in accordance with the Fourth universal definition of myocardial infarction. The study included patients with myocardial infarction type 1 according to the clinical classification of this definition. The points of reference are: 1st - the day of admission to the hospital, 2nd - the day of discharge, 3rd - 12 months after the development of MI. At all three stages of the study (reference points), a general clinical examination was conducted using an assessment of complaints and clinical status. In addition a laboratory examination with a general and biochemical blood test, a general urinalysis, an ECG (on the day of admission at the prehospital stage and / or upon admission to the hospital), X-Ray of chest organs. Echocardiography (Echo-CG) was performed during hospitalization (5-10 days) and after 12 months using the Esaot Maylab 90 diagnostic complex for ultrasound studies in accordance with the recommendations of the American Echocardiographic Society.

Selective coronary angiography was carried out in accordance to the method of F. M. Sones (1959) and M. Judkins (1967), on days 1–3 from the development of symptoms of acute coronary syndrome (ACS) using an Allura CV20 angiographic device from Philips with image fixation on a computer. The risk assessment of unfavorable hospital outcomes was carried out using the TIMI (Thrombolisis In Myocardial Infarction) scale for STEMI - TIMI Risk Score STEMI (Morrow DA, 2000) and GRACE (Global Registry of Acute Coronary Events, 1999-2009): Grace Score 1.0, which allows to predict the risk of deaths at hospital stages with conservative tactics and a 6-month risk of adverse outcomes and an updated Grace Score 2.0, which allows assessing the one-year and three-year risk. Statistical analysis was carried out using the "Statistical Package for the Social Sciences" (SPSS), version 22.0 (2013) and a Microsoft Excel IBM spreadsheet, as well as using the author's odds ratio calculator with the advice of a Doctor of Physical and Mathematical Sciences, Head of the Department of Applied Mathematics Novosibirsk State University of Architecture and Civil Engineering (NGASU), prof. Yu. E. Voskoboinikova.

Evaluating the information given by the GRACE scale in assessing a one-year risk of an adverse vascular event in patients with STEMI. It was found that in 55% of cases, patients at high risk on the GRACE scale did indeed have a fatal or non-fatal cardiovascular event during the observed period (1 year); in patients with intermediate risk, the prognosis was confirmed in 25% of the cases. Sensitivity coefficient = 0.39, specificity coefficient = 0.55. accuracy factor = 0.43

The calculator is a mathematical formula (regression model) programmed in an Excel spreadsheet processor, to determine the annual forecast of STEMI. The author's mathematical model of multivariate forecasting was first built. Correlation analysis of the data was performed to quantify the relationship between these factors and outcomes. Of the 16 factors, the following six factors are significantly correlated with outcome (with variable numbers assigned to them):

X1 is the patient's age;

X2 - admission tachycardia;

X3 - left ventricular ejection fraction;

X4 - anterior localization of myocardial infarction;

X5 - fasting blood plasma glucose before discharge;

X6 is the вчСРП measured on admission.

The calculated pair correlation coefficients for these factors are shown in Table 1.

Table 1

Calculated pair correlation coefficients

	y initial	*x1*	*x2*	*x3*	*x4*	*x5*	*x6*
y initial	1	—	—	—	—	—	—
x1	0,295	1	—	—	—	—	—
x2	0,223	0,164	1	—	—	—	—
x3	0,289	0,081	–0,073	1	—	—	—
x4	0,246	0,140	–0,029	0,141	1	—	—
x5	0,248	0,213	0,112	0,101	0,234	1	—
x6	0,268	0,061	0,158	–0,072	0,164	0,076	1

Note that these variables are weakly correlated with each other, and this prevents the appearance of the multicollinearity effect of the regression model, which negatively affects the accuracy of the calculated model coefficients. Therefore, all of the above variables can be included in the desired regression model.

Since the dependent variable Y - takes only two values (1 - an unfavorable outcome, a conventional designation of ни, 0 - a favorable outcome, a conventional designation of a BI), a logistic regression model was adopted as a mathematical model that calculates the probability of an unfavorable outcome.

In general terms, this model is defined by the expression:

$$p(X) = \frac{1}{1+e^{-z(X)}},$$

Where $z(X) = \beta_0 + \sum_{j=1}^{6} \beta_j \cdot X_j$; β_j - unknown coefficients of the regression model; X_j - independent variables (factors) of the model.

It can be seen that the value $p(X)$ can vary from 0 ($z(X) = -\infty$) to 1 ($z(X) = +\infty$) and therefore the value $p(X)$ is interpreted as the probability of an unfavorable outcome.

To predict the values of a variable Y (0 or 1), the following rule is used:

$$Y = \begin{cases} 0, & \text{если } p(x) \le C_p; \\ 1, & \text{если } p(x) > C_p, \end{cases}$$

Where C_p – threshold value $(0 < C_p < 1)$.

It is obvious that the accurate characteristics of the regression model C_p depend on the choice of the threshold value. The choice of this value will be discussed later.

For the variables defined above, the logistic model is:

$$p(X) = \frac{1}{1+e^{-\left[\beta_0+\beta_1X_1+\beta_2X_2+\beta_3X_3+\beta_4X_4+\beta_5X_5+\beta_6X_6\right]}}$$

Since the coefficients β_j are unknown, the corresponding estimates are calculated b_j for them and the sample (experimental) logistic regression equation takes the form:

$$\hat{p}(X) = \frac{1}{1+e^{-\left[b_0+b_1X_1+b_2X_2+b_3X_3+b_4X_4+b_5X_5+b_6X_6\right]}}$$

Where $\hat{p}(X)$ - assessment of the probability of an unfavorable outcome.

Typically, the least squares method is used to calculate beta scores. Unfortunately, the Excel spreadsheet processor does not have a built-in function that allows you to directly calculate beta scores, or to evaluate the precision of the calculated scores. Therefore, finding these estimates was carried out using the REGRESSION module of the statistical package IBM SPSS version 22, where this possibility exists.

To check the adequacy of the logistic model, three characteristics are used

- Sensitivity coefficient $K_{чув}$ - an assessment of the probability of correct prediction of an unfavorable outcome;

- Coefficient of specificity $K_{спец}$ - an assessment of the probability of correct prediction of a favorable outcome;

- Accuracy coefficient $K_{точ}$ - an assessment of the probability of correctly predicting an unfavorable outcome and correctly predicting a favorable outcome.

To calculate these coefficients, we will use the following four-field table (see table 2).

Table 2

Four-field table for calculating the probability coefficients of the accuracy of the prediction

Initial	Prediction result		In total
	Favorable result БИ (0)	unfavorable result НИ (1)	
БИ (0)	a – number of patients БИ and prediction result БИ	b – number of patients БИ and prediction results НИ	a + b – the total number of patients with БИ
НИ (1)	c – number of patients НИ and prediction result БИ	d – number of patients НИ and prediction result НИ	c + d – the total number of patients with НИ

Then the coefficients of sensitivity and specificity are calculated as follows:

$$K_{чув} = \frac{d}{c+d};$$

$$K_{спец} = \frac{a}{a+b};$$

$$K_{точ} = \frac{a+d}{a+b+c+d}.$$

Obviously, the values of quantities a,b,c,d and consequently, the magnitude of the coefficients $K_{чув}$, $K_{спец}$, $K_{точ}$, depend on the threshold of C_p value included in condition (2). How to choose this threshold? On the first hand, with underestimated values, we obtain highly sensitive prediction of ни or a high prediction with a small probability (risk) of missing ни, but this can lead to unreasonable treatment with the use of expensive drugs and possibly serious side effects. On the other hand, with overestimated values C_p, we obtain highly specific prediction, but the risk of missing ни with all the ensuing consequences increases. Therefore, the choice of the threshold C_p value for prediction using a logistic model is of great importance. In literature, it's recommended to choose the value C_p from the condition of the maximum value $K_{точ}$. For this choice, it is necessary to calculate the values $K_{точ}$ at different values of the threshold value C_p. For this, the following calculations were performed.

Regression equations (1.4) were constructed using the REGRESSION module of the SPSS package for a spatial sample of 124 patients, and then, by changing the threshold values C_p, the coefficient $K_{точ}(C_p)$ was calculated (as a function of the threshold C_p), and then the value $\hat{C}_p$ at which the function $K_{точ}(C_p)$ took the maximum value was found. Figure 3.7 shows the values of the function $K_{точ}(C_p)$. Graphically, it can be determined that for $\hat{C}_p = 0.35$, the accuracy coefficient takes the maximum value. Note that the accuracy of such a graphical calculation of $\hat{C}_p$ is quite sufficient for the practical construction of logistic models.

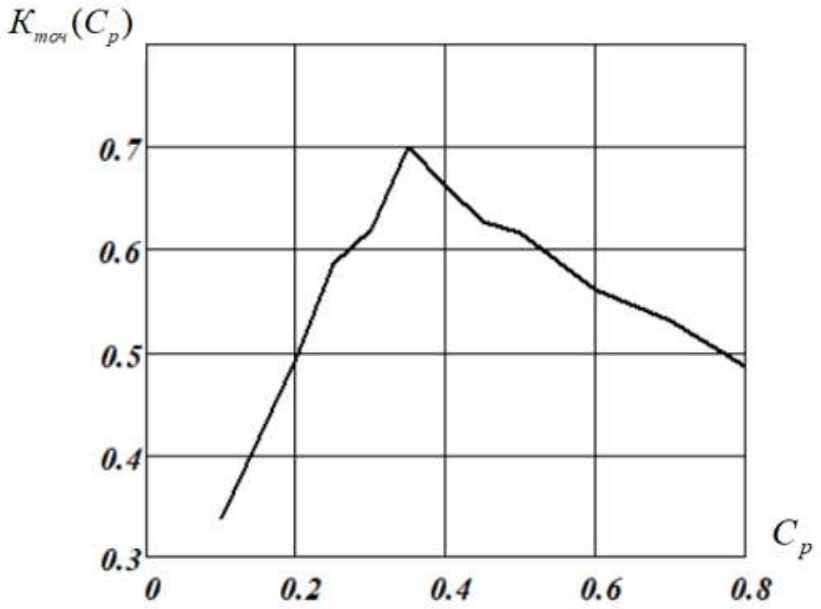

Figure 1 - Graph of the values of the accuracy coefficient

Let's move on to calculate the coefficients b_j in the equation (1.4) of the logistic regression. To do this, we turn to the REGRESSION module of the SPSS statistical package. The results of this module are shown in Figure 3.8 and in a more convenient form are shown in Table 3.

Переменные в уравнении

		B	Знач.	Exp (B)
Шаг 1[a]	VAR00002	,047	,063	1,048
	VAR00003(1)	-,389	,061	,678
	VAR00005(1)	-1,900	,029	,150
	VAR00006	,445	,031	1,560
	VAR00007	,074	,054	1,077
	VAR00008	,093	,025	1,097
	Константа	-2,472	,028	,084

a. Переменные, введенные на шаге 1: VAR00002, VAR00003, VAR00005, VAR00006, VAR00007, VAR00008.

Figure 2 - Screenshot with the results of the REGRESSION module

Table 3

The calculated coefficients of the regression equation

coefficient	value	P-coefficient value
b_0	–2,474	0,028
b_1	0,047	0,063
b_2	–0,389	0,061
b_3	–1,900	0,029
b_4	0,445	0,031
b_5	0,074	0,054
b_6	0,093	0,025

Table 3 shows the calculated coefficients and shows the corresponding P-values for these coefficients. Having set the significance level, we see that all the reduced P-values are less, and therefore, all the calculated coefficients are significant and can be included in the regression equation (1.4).

We then substitute the calculated coefficients in equation (1.4). We receive the following logistic model:

$$\hat{p}(X) = \frac{1}{1+e^{-Z(X)}}$$

Where

$$Z(X) = -2.474 + 0.047X_1 - 0.462(1-X_2) - 1.900(1-X_3) + 0.878X_4 + \\ + 0.380X_5 + 0.312X_6$$

Substituting the function, we obtain the logistic regression equation:

$$\hat{p}(X) = \frac{1}{1+e^{-\left[-2.474+0.047X_1-0.389(1-X_2)-1.900(1-X_3)+0.445X_4+0.074X_5+0.093X_6\right]}}$$

Using a sample of patients participating in the study, we determine the coefficients $K_{чув}$, $K_{спец}$, $K_{точ}$, at the accepted value of the threshold $C_p = 0.35$. Figure 3 shows the results of forecasting using the constructed model.

Таблица классификации[a]

Наблюденные			Предсказанные		
			VAR00001		Процент правильных
			,00	1,00	
Шаг 1	VAR00001	,00	51	23	68,9
		1,00	14	36	72,0
	Общая процентная доля				68,5

a. Значение отсечения - ,350

Figure 3 - Screen copy of the prediction results for the constructed model

The obtained values will be entered in table 4.

Table 4

Four-field table for calculating coefficients

results	Prediction results		Total
	favorable result БИ (0)	unfavorable result НИ (1)	
БИ (0)	51	23	74
НИ (1)	14	36	50

Using the formulas, we calculate:

$$K_{чув} = \frac{36}{50} = 0.72,\ K_{спец} = \frac{51}{74} = 0.69,$$

$$K_{точ} = \frac{36+51}{124} = \frac{87}{124} = 0.69$$

Considering another characteristic used in the analysis of the logistic model, called characteristic curve (or ROC-curve), which shows the dependence of the number of correct ни predictions on the number of incorrect ни predictions and is a locus of points in a Cartesian coordinate system with coordinates:

$$y_{ROC}\left(C_p\right) = K_{чув}\left(C_p\right),$$

$$x_{ROC}\left(C_p\right) = 1 - K_{спец}\left(C_p\right)$$

which depend on the threshold value. The ideal predictive model should be Г(G in Russian)-shaped and pass through the upper left corner with coordinates (0,1). The closer the characteristic curve goes to this point, the higher the prediction efficiency. Figure 4 shows the values.

The ROC curve for the model (1.10), which is below the ideal ROC curve, and this indicates the average quality of the logistic regression (3).

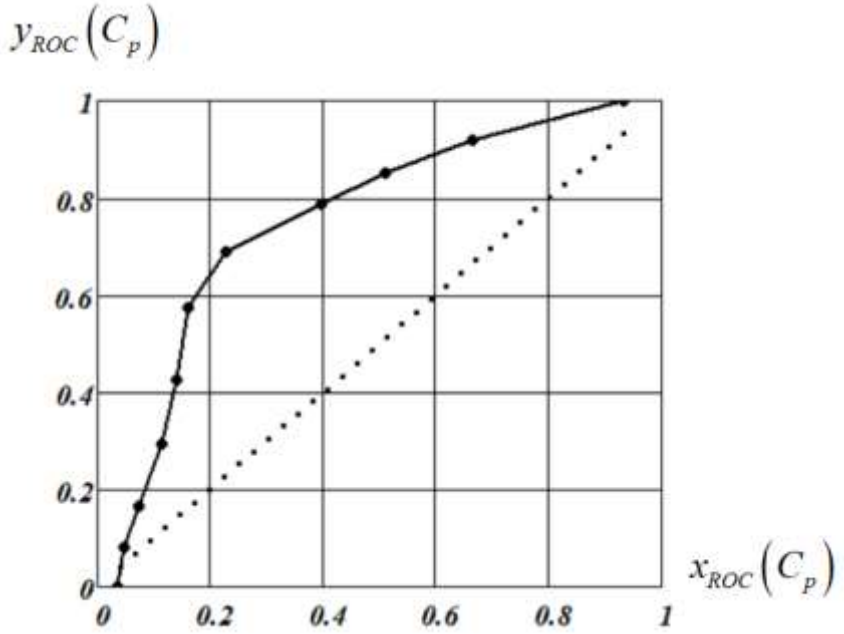

Figure 4– Logistic model ROC curve plot

The characteristic curve can be quantified by calculating the area under it - the AUC coefficient. Approximating the ROC curve with cubic splines and calculating the definite integral (area under ROC curve), we get a value equal to 0.780. The approximate scale of AUC values reflecting the quality of the prediction is as follows:

AUC = 0,9–1,0 – excellent quality;
AUC = 0,8–0,9 – high quality;
AUC = 0,7–0,8 – good quality;
AUC = 0,6–0,7 – medium quality;
AUC = 0,5–0,6 – bad quality.

It is observed that the constructed model is of good quality. Notice, that the ROC curve in the form of a straight dotted line in Figure 4 has an AUC = 0.5.

Conclusion: By generalizing the presented accuracy characteristics ($K_{чув}$, $K_{спец}$, $K_{точ}$, AUC coefficient) of the constructed model (1.9), we can conclude that this model is sufficiently effective to predict outcomes with unfavorable outcomes.

Verification of the adequacy of the constructed regression equation

Although the P-values given in Table 3 indicate the significance of the calculated coefficients, the adequacy of the constructed regression equation was checked, which included the following test.

A new spatial sample of 80 was formed from the database of outgoing patients of the cardiology department of the RSC No. 1 at the GBUZ NSO "GKB No. 1" in September 2019, and the calculation of the probability of an unfavorable outcome and the calculation of the outcome in accordance with the formula (1.9) (at Cp = 0.35). A fragment of the table is shown in Figure 5.

	A	B	C	D	E	F	G	H	I	J
1										
2										
3										
4	Номер	у исходы	возр	ЧСС пост	ФВ 1	лок ИМ	глюк 1	CRP 1	Вероятность P(Z)	Прогнозируемый исход
5	1	1	67	0	0	2	6,72	143,91	*1*	*1*
6	2	0	41	0	0	1	7,63	1,44	*0,16*	*0*
7	3	1	54	0	0	2	5,92	26,12	*0,82*	*1*

Figure 5 - Fragment of the Excel processor table for calculating outcomes in the control group

Table 5 shows the number of initial values of the variable Y and the number of calculated (predicted) values, as well as the percentage of coincidence of these values.

Table 5

Four-field table for assessing the effectiveness of forecasting

Observed (initial) values of a variable *Y*	Predicted (calculated) variable values *Y*		Total number	Percentage of matches
	0	1		
0	33	17	50	66
1	8	22	30	73
Total percentage of matches			80	69

The data in the table allow us to conclude that the proposed predicting method is characterized by high sensitivity and acceptable specificity. Of the 80 examined patients with NSTE-ACS, adverse events within 12 months from the date of NSTE-ACS actually occurred in 30 people (according to the prognosis of the proposed method, it should have occurred in 22 people), there were no adverse events in 50 patients (of which, according to the proposed method should not have had in 33 people). Thus, the sensitivity of the proposed method for predicting unfavorable outcomes was 73%, favorable outcomes - 66%.

Thus, our multivariate model is more informative for predicting a favorable or unfavorable long-term outcome for a particular STEMI patient.

Conclusion: By generalizing the given accuracte characteristics ($К_{чув}$, $К_{спец}$, $К_{точ}$, AUC-coefficient) of the constructed model (1.9), we can conclude that this model is sufficiently effective to predict outcomes with unfavorable outcomes.

Let's make one important remark. Although the constructed logistic regression equation can predict outcomes quite accurately, it does not calculate the "individual" contribution of each disease to this predicted outcome.

The coefficients of equation (1.9) are "averaged" coefficients of the influence of each disease (factor) on the outcome and not taking into account the characteristics of each patient. Obtaining such information about the impact of each disease on the outcome (especially the unfavorable results) would allow the development of an "individual" treatment plan for a particular patient, paying more attention to diseases that significantly affect the outcome.

To define such a disease, we introduce a function determined by the formula:

$$F(x) = 0.047x_1 + 0.462x_2 + 1.900x_3 + 0.878x_4 + 0.380x_5 + 0.312x_6$$

Note that lowercase letters denote specific (observed) values of the factors of a given patient, as opposed to capital letters in the model equation (1.9.), Which denote variables. Summing up the influence of all diseases of a given patient on the outcome allows us to name this function as the function of "severity of patient's risk factors" or "function TFRP". Denoting the value of this function for a particular patient as S and introduce the following "Personal disease coefficients", which reflect the relative contribution of each patient's disease to the value of the ТБП function:

$$S_1 = \frac{0.047x_1}{S}$$ – influence of the patient's age; (1.13)

$$S_2 = \frac{0.462x_2}{S}$$ – effect of left ventricular ejection fraction; (1.14)

$$S_3 = \frac{1.900x_3}{S}$$ – effect of left ventricular ejection fraction; (1.15)

$$S_4 = \frac{0.878x_4}{S}$$ – influence of the anterior localization of myocardial infarction; (1.16)

$$S_5 = \frac{0.380x_5}{S}$$ – the effect of fasting plasma glucose before discharge; (1.17)

$$S_6 = \frac{0.312x_6}{S}$$ – impact of вчСРП measured on admission. (1.18)

Despite the computational simplicity of the constructed model and coefficients (1.12–1.18), for their effective application in practice, convenient and understandable software is required. It was developed and implemented in an Excel spreadsheet processor and was named "Patient's Personal Calculator".

Figure 6 shows a fragment of the interface for entering the values of 6 factors included in the constructed regression model. Cells D1-D7 contain the coefficients of the model and DO NOT HAVE TO CHANGE them.

Figure 7 shows a fragment of the interface that shows the results of the prediction of an unfavorable result.

Figure 8 shows a fragment of the interface, which shows the results of calculating personal coefficients.

Figure 9 shows a graphical representation of the calculated personal coefficients (including the patient's age).

Figure 10 shows a graphical representation of the calculated personal coefficients (excluding the patient's age).

	A	B	C	D	E	F	G
1			конст	-2,474			
2			VAR00002	,047	x1		
3			VAR00003(1)	-0,389	x2		
4			VAR00005(1)	-1,900	x3		
5			VAR00006	0,445	x4		
6			VAR00007	,074	x5		
7			VAR00008	0,093	x6		
8							
9		1	2	3	4	5	6
10		Возраст	ЧСС пост	ФВ	Лок ИМ	Глюкоза	CRP 1
11		61	0	0	2	5,2	3,71
12		Исходные данные для калькулятора (6 величин)					

Figure 6 - Fragment of Excel for entering the initial data

	порог=	0,35
Исход НЕ БЛАГОПРИЯТНЫЙ		
Z(X)	P(Z)	Y предск
-0,273	0,43	1

Figure 7 - A fragment of Excel for displaying the results of calculating the results

13					
14				Слагаемые ТБП	Персональные коэффициенты
15	1	возр	2,867	2,867	0,419
16	2	ЧСС пост	-0,389	0,000	0,000
17	3	ФВ	-1,9	0,000	0,000
18	4	лок ИМ	0,89	2,152	0,315
19	5	Глюк	0,386	0,386	0,056
20	6	CRP1	0,34503	1,431	0,209
21			*-0,275*	*6,836*	1,000
22					

Figure 8 - Excel fragment for displaying the results of calculating personal coefficients

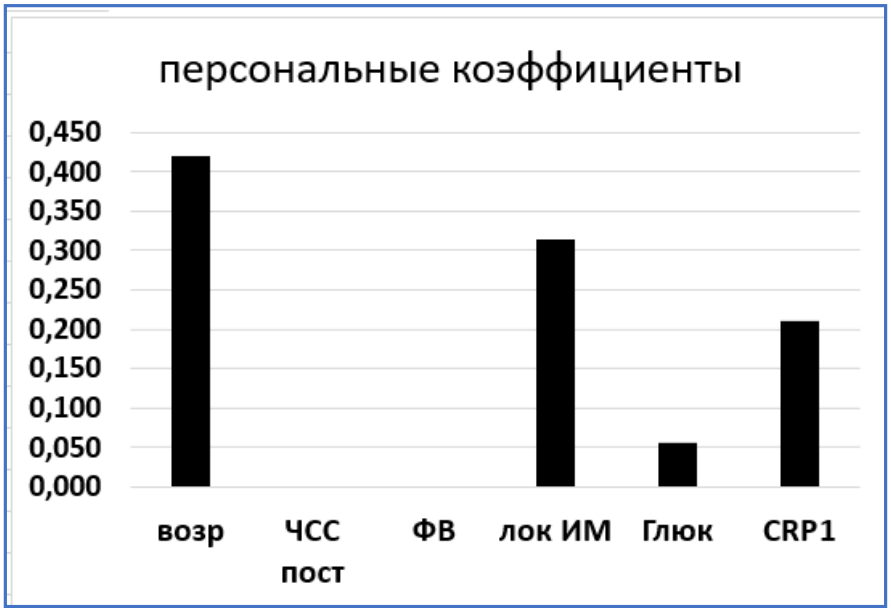

Figure 9 - Graphical representation of personal odds

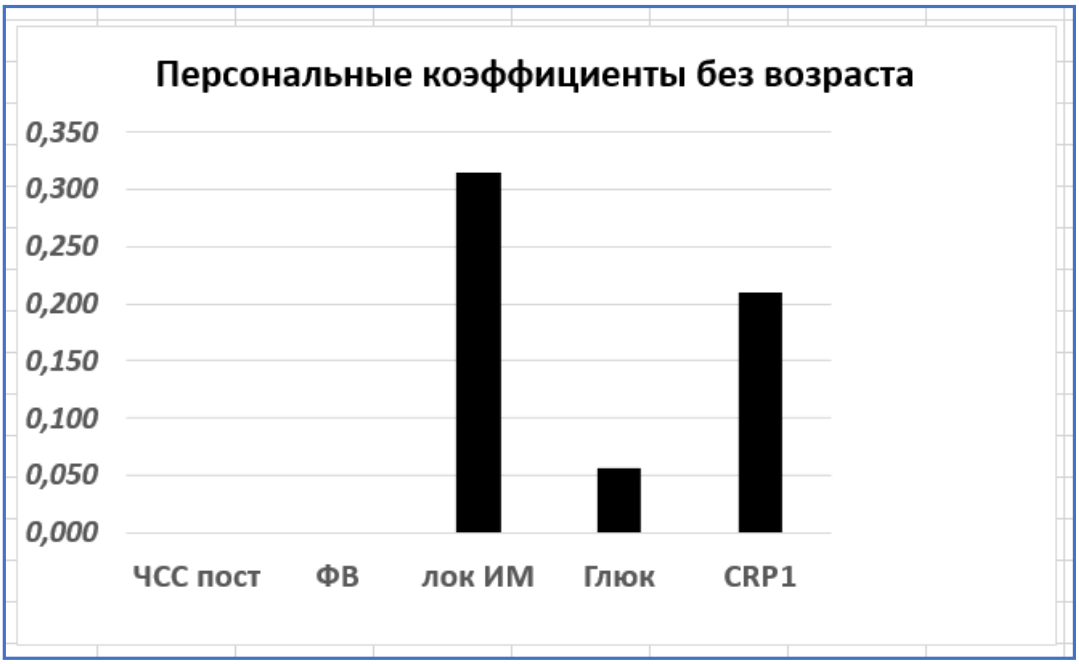

Figure 10 - Graphic representation of personal odds

From these figures, it is seen that data entry and interpretation of calculating results will not present difficulties for ordinary computer users.

Discussion:

The developed method for assessing annual outcomes after acute myocardial infarction with persistent elevation of the ST segment on an ECG using an annual prognosis calculator with personal risk factor coefficients is of good quality (AUC coefficient is 0.780), while the GRACE risk model has a low predictive ability for high risk 55%, and for intermediate 25%, respectively.

As is known, clinical guidelines recommend the use of the TIMI and GRACE risk scales. Both scales are comparable for predicting inpatient mortality, and GRACE for STEMI also provides predictive value at 6 months after discharge. A number of researchers propose to include an assessment of LVEF, the presence of multivessel disease, and the completeness of coronary revascularization.

This paper compares the results of assessing the one-year prognosis after a myocardial infarction using the author's "personal patient calculator" with the GRACE risk measurement. As already mentioned, the prognosis was confirmed in 55% of patients with high risk on the GRACE scale, and in patients with intermediate risk, the prognosis was confirmed in 25% of the cases. According to the author's calculator, the predicting accuracy was almost 79% for unfavorable results, and 70% for favorable results.

Thus, the proposed author's "personal patient calculator" is more informative for predicting a favorable or unfavorable long-term outcome for a patient with acute myocardial infarction. High informative content, specificity, sensitivity and accuracy of the author's method is due to the fact that he takes into account not

only cardiovascular death and myocardial infarction, like GRACE, but also stroke, hospitalizations due to repeated ischemia, unscheduled coronary and non-coronary revascularization, developed on the basis of a survey of Russian patients, taking into account a one-year period, and not just the first six months, like GRACE, since there is a high risk of a fatal and serious non-fatal event in patients after MI persists for a year. The proposed formula makes it possible to predict the contribution of each risk factor to a long-term outcome, which implies personalized work with each patient and modeling the outcome in terms of time and changing components of its prognosis.

The GRACE model has three levels of risk - high, moderate and low. It turns out that patients with a moderate risk of an unfavorable outcome are a group that is not very clear for a practitioner in terms of secondary prevention, and this is the main goal of risk metrics.

It should be noted that the proposed calculator is easy to use, as it is implemented in an Excel spreadsheet processor, so any practitioner can use it.

Conclusion:

This study demonstrates the role of the proprietary calculator for the annual prognosis of the risk of unfavorable cardiovascular events with personal coefficients of risk factors in patients after undergoing STEMI. The author's calculator was developed on the basis of data from Russian patients and takes into account a one-year period, and not only the first six months, as when using the GRACE scale, since a high risk of cardiovascular events in patients after STEMI persists for a year. The calculator takes into account the total cardiovascular risk: cardiovascular death, acute myocardial infarction, stroke, hospitalization for ischemia, unscheduled coronary and non-coronary revascularization. The proposed method allows you to personally simulate the outcome in real time for each patient, which ultimately will affect the quality of life in patients who have had myocardial infarction.

PRINCIPLES AND CONSTANTS OF THE GOLDEN PROPORTION AS A CRITERION IN DONOSOLOGICAL DIAGNOSTICS OF THE FUNCTIONAL STATES OF THE BODY AND IN THE ASSESSMENT OF THE PROBABILITY OF THEIR CHANGES

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Abstract

A functional state is a complex of properties of an organism that determines the level of its vital activity. The construction of human functional structures is based on the laws of nature. The golden proportion is a universal natural law and the highest manifestation of the structural and functional perfection of the organism, and has properties and principles: self-development, self-organization and self-regulation, balance and stability. It is found in the anatomical and physiological parameters of the human body, is a method for finding an extremum in solving problems of their optimization. Proceeding from the fact that the functional state of the cardiovascular system is an integral indicator of the general state of the body and its adaptation, as a process of searching for the optimal functional state, we studied this indicator in 43 young people. At the same time, it was found that the subjects under conditions of functional rest and in a satisfactory state of compensatory-adaptive capabilities, i.e. in prenosological conditions, their adaptive potential lies in the range of two values of the golden proportions (F = 1.618; F2 = 2.618). Thus, the golden proportions form the boundaries of the functional corridor, outside of which there is a change in the prenosological state of the body, namely, with an adaptive potential of less than 1.618, a physiological norm takes place, and with more than 2.618, premorbid states. In this regard, it is proposed a scale for assessing the functional state, as well as an index of the likelihood of developing a premorbid state in an individual's body, based on the principles and constants of the golden ratio. The discriminatory ability and sensitivity of the proposed scale to the functional states of the organism were assessed.

Keywords: functional state, adaptive potential, health levels, golden ratio constants, harmonization, optimization, assessment scale.

The relevance of research

International standards for the provision of medical care provide for the implementation of preventive measures aimed at preventing the occurrence of diseases already at the stage of their initial manifestations. At the same time, the existing system of primary prevention is still devoid of the most important element - objectification of the assessment of the functional state of the body at the level of a pre-morbid state, when, as a result of the inconsistency of the body's capabilities, the prerequisites for the development of the pathological process arise. Such a gap in the system of primary prevention is intended to fill the methodology of prenosological diagnostics, according to which the development of clinical forms of diseases is preceded by quite definite disorders of the functional state (FS) of the body, in which the nonspecific component of the general adaptation syndrome manifests itself in the