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Novel score for mortality risk prediction 6 months after acute coronary syndrome

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Aim. To create a prediction score for assessing the mortality risk 6 months after hospitalization with acute coronary syndrome (ACS).

Material and methods. Based on the results of ACS RECORD-3 register (Russia), we determined independent mortality predictors 6 months after ACS by performing multivariate regression analysis in patients discharged alive from the hospital with known outcomes.

Results. The following predictors were obtained during the analysis: non-prescription of aspirin at discharge (odds ratio (OR) 5,8; 95% confidence interval (CI) 2,3-15,0; p<0,0001), newly diagnosed heart failure, pulmonary edema or shock in a hospital (OR 5,7; 95% CI 2,6-12,7; p<0,0001), age ⩾75 years (OR 5,3; 95% CI 2,7-10,6; p<0,0001), non-prescription of beta-blockers at discharge (OR 5,0; 95% CI 2,3-10,8; p<0,0001), in-hospital management without immediate percutaneous coronary intervention (PCI) (primary PCI during ST-segment elevation ACS or PCI during the first 72 hours in non-ST-segment elevation ACS) (OR 3,9; 95% CI 1,6-9,8; p=0,004), the initial serum creatinine ⩾100 μmol/L (OR 3,1; 95% CI 1,6-6,1; p=0,001), body mass index <30 kg/m^2 (OR 2,8; 1,2-6,3; p=0,014). Each of them was evaluated at one point and was a component of the RECORD-6 score. Prediction sensitivity and specificity for the new score were 73,3% (95% CI 60,1-83,5) and 71,4% (95% CI 68,9-73,7), respectively; prediction accuracy, estimated as the area under the ROC curve was 0,931 (95% CI 0,897-0,964). The cut-off point was considered 3 points, which had the best ratio of prediction sensitivity and specificity. The mortality after 6 months with a value of <3 points was 1,6%, and with a value of ⩾3 points — 10,1% (relative risk (RR) 0,16; 95% CI 0,09-0,28; p<0,0001), and the mortality after 12 months was 7,8% and 22,5%, respectively (RR 0,35; 95% CI 0,25-0,49; p<0,0001). Relative to the GRACE risk score for 6-month mortality, the prediction value of the RECORD-6 score was at least no worse.

Conclusion. The novel RECORD-6 risk score is an accurate and simple prediction tool for assessing the mortality risk 6 months after discharge from the hospital. The prediction accuracy of the RECORD-6 risk score is not lower the GRACE risk score.

Key words: acute coronary syndrome, prediction score, 6 months, RECORD, GRACE, long-term outcomes, death.

Relationships and Activities: not.

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Determining the prognosis in patients with acute coronary syndrome (ACS) is an important and inherent element of the entire treatment process. Given the many factors affecting the prognosis and their "weight", in practice, the prognosis often requires the use of special prognostic scales, combining several significant predictive factors. In ACS, for example, the GRACE and the TIMI are the most commonly used risk scores. Current clinical guidelines suggest the use of PRECISE-DAPT and DAPT scores to determine the risk of bleeding and the duration of dual antiplatelet therapy [1].

At present, prognostic scores are rarely used to assess the long-term risk of adverse events. Although the current version of the GRACE risk score is highly sensitive and specific for predicting the 6-month mortality risk after ACS [2], it is also little used in practice. At the same time, the importance of assessing long-term risk, especially after discharge from the hospital after ACS, is obvious, since this data can be potentially useful for subsequent outpatient management.

The aim of this analysis was to create a prediction score for 6-month mortality after hospitalization with ACS.

Material and methods

The analysis was performed based on the data of ACS RECORD-3 register (Russia) — a short-term prospective observational study, which included all hospitalized patients for 1 month (March-April 2015, 47 hospitals of 37 Russian cities; n=2370). Detailed information on the features and the main results of the RECORD-3 register was presented in previous publications [3].

Follow-up 6 months after ACS onset was carried out in 34 participating hospitals (n=2009) by telephone surveys. Data on 454 patients were not received. Data on 113 patients who died during hospitalization were excluded. Thus, the present analysis was performed on 1433 survivors after hospitalization, about which there were data on adverse events 6 months after the ACS onset.

The parameters of the novel risk score were independent predictors of 6-month mortality after the ACS onset and hospitalization.

Statistical processing was performed using software packages Statistica 10.0 and IBM SPSS Statistics 22. Discrete variables were compared using Yates's chi-squared test. To identify factors associated with 6-month post-ACS mortality, a step-by-step multivariate logistic regression analysis was performed. The studied factors were included in multivariate regression analysis if they were associated with the outcome with a significance level of $p<0,1$. The estimation of the relative risk was performed using the online calculator on the website www.medstatistic.ru. Comparison of the prognostic value of the risk scores was carried out by comparing the areas under ROC curves and using the McNeil test (www.vassarststs.net/roc_comp.html).

Results

Results of multivariate regression analysis. According to a univariate regression analysis, more than 50 anamnestic, laboratory, and clinical factors, as well as factors related to the characteristics of treatment and outcomes during hospitalization, were associated with the 6-month post-ACS mortality and were included in multivariate regression analysis. Independent predictors of 6-month mortality, identified by multivariate analysis, are presented in Table 1.

Creation of a prognostic score. The creation of the prognostic score was carried out in two fairly similar ways. According to one of them, each factor identified in multivariate regression analysis was assigned a value equal to its average odds ratio value. Thus, there was a score with a minimum value of 0 and a maximum value of 32 points ("advanced version score"). In another way, each factor was assigned 1 point, and there was a minimum value of 0 and a maximum value of 7 points ("simplified version score"). The prognostic value of these scores was compared using the ROC curve. The area under the ROC curve for the "advanced version score" was 0,935 (95% confidence interval (CI) 0,900-0,970), and for the "simplified version score" — 0,931 (95% CI 0,897-0,964) (Figure 1). The statistical difference of these values was not significant. For the "advanced version score", the prognostic sensitivity was 78,3% (95% CI 65,5-87,5), and specificity — 57,6% (95% CI 54,9-60,2). For the "simplified version score", the prognostic sensitivity was 73,3% (95% CI 60,1-83,5), and specificity — 71,4% (95% CI 68,9-73,7).

Thus, given the absence of significant difference in the area under the ROC curves of two presented versions, the similar sensitivity and specificity values, and undoubted simplicity in the calculations of "simplified version score", we chose it as a novel prognostic score, where each factor is assigned 1 point (Table 2).

Assessment of the RECORD-6 score prognostic value. The proportion of non-surviving patients depending on the RECORD-6 score data is presented in Figure 2. It can be seen that with increasing scores, the mortality rate progressively raised.

The cut-off point for the RECORD-6 score determining the low and high mortality risk after 6 months was value of 3 points. According to the ROC curve

Table 1

Independent predictors of 6-month mortality after hospitalization with ACS

Factor	ОШ	95% ДИ	p
Non-prescription of aspirin at discharge	5,883	2,302-15,035	<0,0001
Newly diagnosed heart failure, pulmonary edema or shock in a hospital	5,734	2,585-12,717	<0,0001
Age ⩾75	5,328	2,697-10,597	<0,0001
Non-prescription of beta-blocker at discharge	4,984	2,297-10,815	<0,001
In-hospital management of ACS without immediate PCI (primary PCI during ST-segment elevation ACS or PCI during the first 72 hours in non-ST-segment elevation ACS)	3,902	1,559-9,770	0,004
Serum creatinine upon admission ⩾100 μmol/L	3,091	1,555-6,144	0,001
Body mass index <30 kg/m^2	2,788	1,236-6,292	0,014

Abbreviations: OR — odds ratio, CI — confidence interval, PCI — percutaneous coronary intervention.

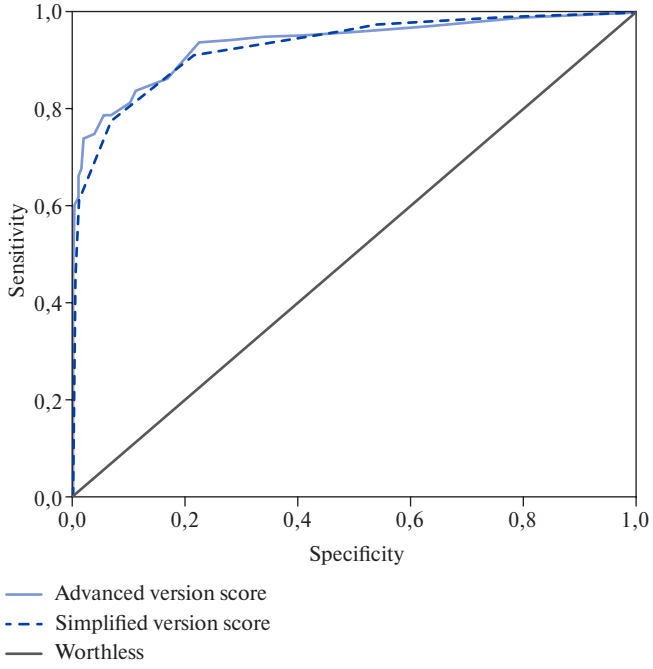

Figure 1. ROC curves for advanced and simplified versions of RECORD-6 score.

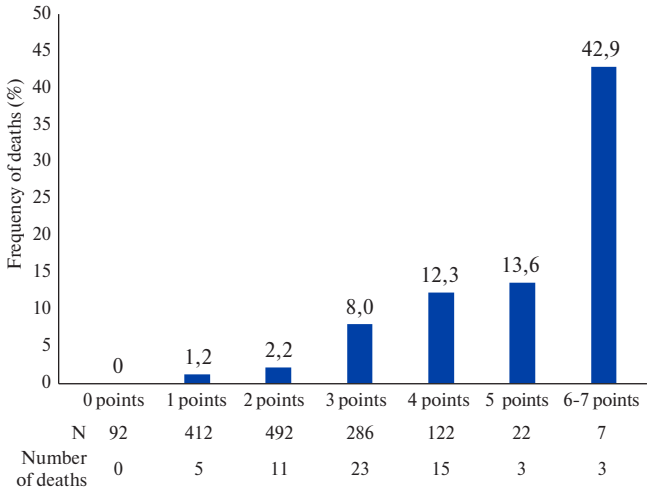

Figure 2. The relationship of the values on the RECORD-6 score with 6-month post-ACS mortality.

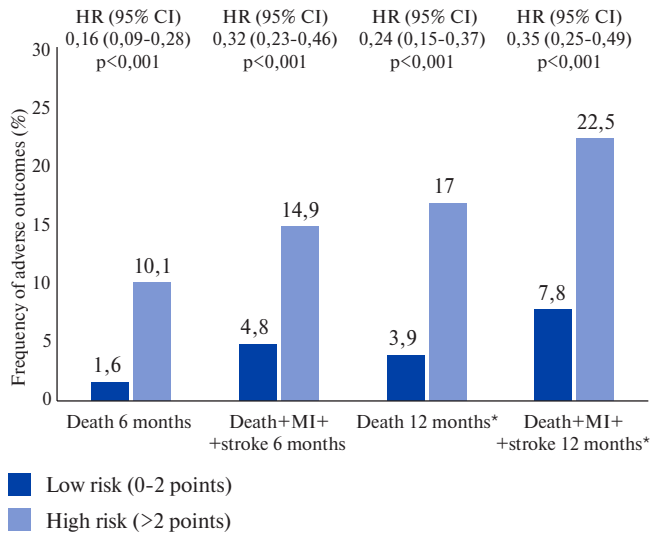

Figure 3. The incidence of long-term adverse events in low- and high-risk patients according to the RECORD-6 score.
Note: * — in patients with outcomes recorded after 12 months (n=966).
Abbreviations: HR — hazard ratio, CI — confidence interval, MI — myocardial infarction.

analysis, it has the best proportion of prognostic sensitivity and specificity. Thus, the value of <3 points indicates a low risk of long-term adverse events, and the value of ⩾3 points — high risk. The incidence of adverse events in patients with high and low risk according to the RECORD-6 score is presented in Figure 3.

It can be seen that the high risk on the RECORD-6 score was associated with a significantly higher rate of 6- and 12-month mortality after hospitalization, as well as serious adverse events (death, myocardial infarction or stroke) over the same period of time.

Figure 4 and Table 3 show a comparison of the prognostic values of the RECORD-6 and the 6-month GRACE risk score, expressed as the area under the ROC curve. Although the area under the ROC curve was visually larger for the RECORD-6 score (espe-

Table 2

Factors and their values for the novel RECORD-6 score

	Factor	Score
Data on admission or close to admission	Body mass index <30 kg/m^2	1
	Age ⩾75	1
	Serum creatinine upon admission ⩾100 μmol/L	1
In-hospital events	In-hospital management of ACS without immediate PCI (primary PCI during ST-segment elevation ACS or PCI during the first 72 hours in non-ST-segment elevation ACS)	1
	Newly diagnosed heart failure, pulmonary edema or shock in a hospital	1
Prescriptions at discharge	Non-prescription of beta-blocker at discharge	1
	Non-prescription of aspirin at discharge	1
Maximum score		7

Abbreviations: OR — odds ratio, CI — confidence interval, PCI — percutaneous coronary intervention.

Table 3

Areas under the ROC curves of the RECORD-6 and the 6-month GRACE risk score

	Area under the ROC curve	95% CI	p
All patients			
RECORD-6	0,872	0,847-0,909	0,47
6-month GRACE risk score	0,832	0,796-0,868	
Patients with non-ST-segment elevation ACS			
RECORD-6	0,822	0,770-0,874	0,70
6-month GRACE risk score	0,795	0,738-0,852	
Patients with ST-segment elevation ACS			
RECORD-6	0,931	0,897-0,964	0,46
6-month GRACE risk score	0,865	0,822-0,907	

Abbreviations: CI — confidence interval.

cially in ST-segment elevation ACS), this difference was not statistically significant.

Discussion

This analysis, based on the ACS RECORD-3 register (Russia) was performed, firstly, because of the obvious importance for assessing the risk of long-term adverse events after ACS, secondly, because of the rare practical use of prognostic scores for these purposes (even such accurate and well-validated as the GRACE score) [4, 5], and thirdly, due to the experience in creating the RECORD prognostic score [6]. This score showed a high accuracy in assessing the risk of in-hospital adverse events in patients with ACS, and can also be used for more targeted selection of patients with non-ST-segment elevation ACS for invasive coronary procedures.

The main idea for creating a new prognostic score was to evaluate the long-term prognosis in ACS patients surviving during hospitalization. Exclusion of patients not surviving during hospitalization made it possible to offset the significance of factors of early-stage unfavorable prognosis. The new score was developed according to the standard methodology, where independent predictors of an unfavorable outcome were identified and assigned the score components. As in the above-mentioned RECORD score, two versions of the new score were compared: the advanced one, where the "weight" of each factor was determined by its odds ratio value, and the simplified one, where each factor had the same "weight". Since the simplified version was not inferior to the advanced one in terms of prognostic sensitivity and specificity, it was chosen as a RECORD-6 score. Thus, the new score includes 7 various factors: old age, increased creatinine level, in-hospital management of ACS without immediate percutaneous coronary intervention (PCI), non-prescription of aspirin or beta-blocker, BMI <30 kg/m^2, in-hospital development of heart failure, shock, pulmonary edema.

It seems that there is no need to discuss in detail the individual prognostic value of each factor, especially taking into account that their combination (RECORD-6 score), showed high prognostic accuracy and the value of area under the ROC curve (0,931). Using the ROC analysis, a score of 3 was determined as a cut-off point, dividing the RECORD-6 score into low and high risk. The use of this cut-off point was highly accurate for predicting the 6-month and 12-month mortality rates, and the sum of events (all-cause mortality, myocardial infarction and stroke) after 6 and 12 months.

To assess the value of the RECORD-6 score, it was compared with the 6-month GRACE risk score by comparing the areas under the ROC-curves. Despite the quantitative advantage of the RECORD-6 score, this difference was not significant. It is noteworthy that the most marked advantage of the RECORD-6 score over the GRACE score was among patients with ST-segment elevation ACS. It should be noted that in the original sample of the GRACE register, on the basis of which the 6-month mortality risk score was developed, the accuracy, defined as the area under the ROC curve, was 0,81 [2]. This value is quite similar with the data obtained for GRACE score in our study (0,795). This may indirectly indicate that the patients of the RECORD-3 register are quite typical and characteristic for the population of ACS patients. Therefore, the novel RECORD-6 score is at least no worse than the GRACE score and can be used in clinical practice.

Study limitations. The current analysis has the following limitations:

1) Creating a new prognostic score was not the primary aim of the ACS RECORD-3 register;

2) The results obtained require validation in other independent cohorts of patients with ACS;

3) To use the RECORD-6 score in clinical practice, additional studies and its validation in other cohorts of patients with ACS are required.

Conclusion

1) Based on the ACS RECORD-3 register (Russia), a new risk score for predicting the 6-month all-cause mortality after hospitalization with ACS was created;

2) The novel RECORD-6 score includes 7 components (independent predictors of 6-month mortality after ACS): 1) body mass index <30 kg/m^2, 2) age ⩾75 years, 3) serum creatinine upon admission ⩾100 μmol/L, 4) in-hospital management of ACS without immediate PCI (primary PCI during ST-segment elevation ACS or PCI during the first 72 hours in non-ST-segment elevation ACS), 5) newly diagnosed heart failure, pulmonary edema or shock in a hospi-

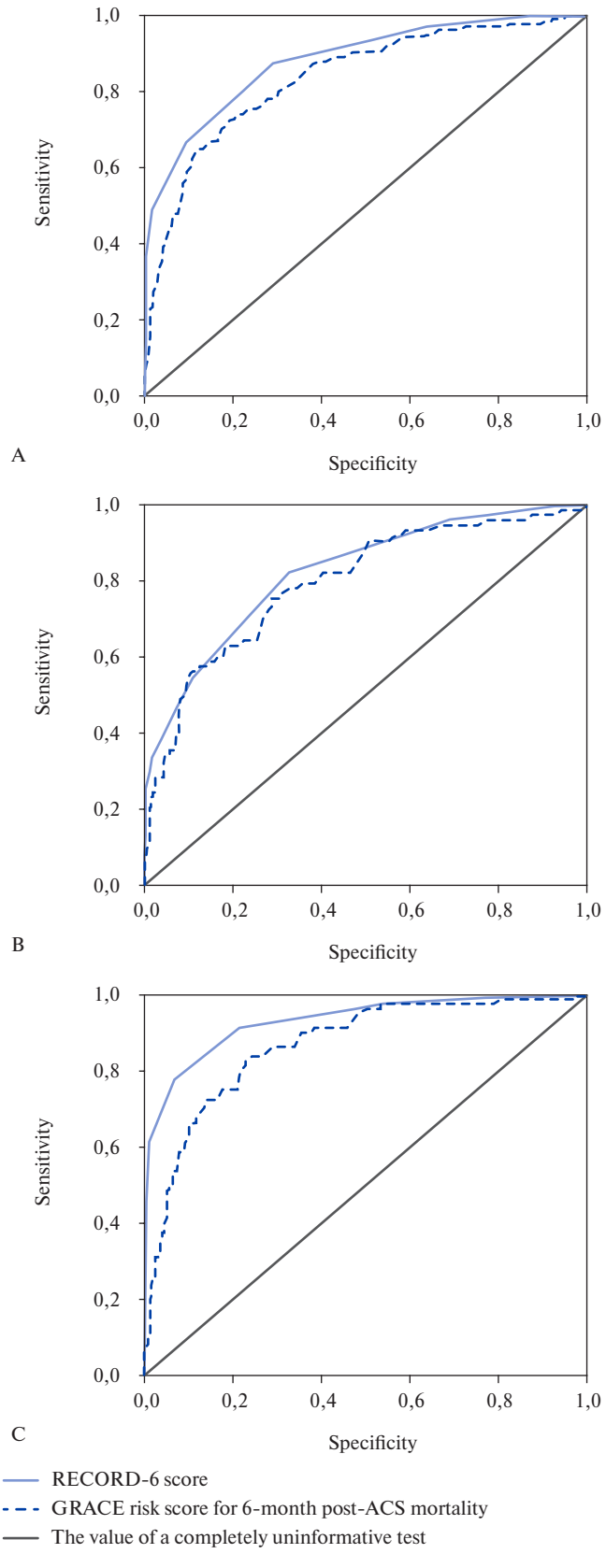

Figure 4 (A, B, C). ROC curves of the RECORD-6 score and the 6-month GRACE risk score for 6-month post-ACS mortality for all patients (**A**), patients with non-ST-segment elevation ACS (**B**) and ST-segment elevation ACS (**C**).

tal, 6) non-prescription of aspirin at discharge; and 7) non-prescription of beta-blocker at discharge;

3) Relative to the GRACE risk score for 6-month mortality, the prognostic value of the RECORD-6 score is at least no worse.

4) A score of 3, considered as a cut-off point, allows accurately dividing the patients into low and high risk groups in relation to 6- and 12-month mortality, as well as predicting the sum of events (all-cause mortality, myocardial infarction and stroke) after 6 and 12 months of the ACS onset.

Relationships and Activities: not.

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