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Comparison of the prognostic significance of the complications according to short-term scales in patients with Non-ST-segment elevation acute coronary syndrome without percutaneous coronary intervention

Alnaser M., Sychev I. V., Pushkina Y. A., Goncharova L. N.
National Research Ogarev Mordovia State University, Saransk, Russia.

AUTHORS

Alnaser Murkhaf, PhD student, Department of Faculty Therapy with courses of physiotherapy, physical therapy of the National Research Ogarev Mordovia State University, Saransk, Russia. ORCID: 000-002-5317-339X
Ivan V. Sychev, PhD student, Department of Faculty Therapy with courses of physiotherapy, physical therapy of the National Research Ogarev Mordovia State University, Saransk, Russia. ORCID: 0000-0003-0227-2651
Yana A. Pushkina*, PhD student, Department of Faculty Therapy with courses of physiotherapy, physical therapy of the National Research Ogarev Mordovia State University, Saransk, Russia. ORCID: 0000-0001-7505-2698
Lyudmila N. Goncharova, MD, PhD, professor, Department of Faculty Therapy with courses of physiotherapy, physical therapy of the National Research Ogarev Mordovia State University, Saransk, Russia. ORCID: 0000-0002-4324-9071

Abstract
This study aimed to compare the short-term prognosis of fatal and nonfatal complications using GRACE (Global Registry of Acute Cardiac Events risk score), TIMI (Thrombolysis In Myocardial Infarction), PREDICT (PREdicting risk of Death In Cardiac disease Tool), PURSUIT (Platelet Glycoprotein IIb-IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy) and RECORD scales in patients with Non-ST-segment elevation acute coronary syndrome (NSTE-ACS) without percutaneous coronary intervention (PCI).
Methods. 122 patients admitted to the Mordovian Republican Central Clinical Hospital" with a referral diagnosis of NSTE-ACS were examined. The peculiarity of this sample is the absence of primary PCI while the patient was in the hospital. Absence of primary PCI was explained in 14 (11.5%) patients by the refusal of coronary angiography (CAG) (due to age), in 8 (6.5%) patients due

* Corresponding author. Tel.: +7 (960) 339-0446;. E-mail: frolkina1992yana@mail.ru

to intolerance of contrast agent or analgesic medication. All other 100 patients from this group underwent CAG, where intact coronary vessels were detected in 27 (27%) patients, in 42 (42%) patients the degree of stenosis was less than 50% and in 31 (31%) patients (all patients with type 2 diabetes) a distal type of coronary lesion was detected.

Results. When comparing the effectiveness of prognostic significance of short-term fatal and nonfatal complications, as well as the prognosis assessment regardless of the type of adverse outcome in ACS patients without PCI, GRACE scale showed the highest sensitivity and specificity compared with short-term RECORD, PREDICT, TIMI and PURSUIT scales used in this study. The TIMI and RECORD scales showed efficacy of short-term prognosis only for fatal complications in this category of patients.

Conclusion. Taking into account the results of this study in NSTE-ACS patients without PCI, the GRACE scale was recommended to assess the prognostic significance of short-term complications regardless of the type of adverse outcome.

Keywords: NSTE-ACS without PCI, short-term prognostic scales — GRACE, RECORD, PREDICT, TIMI, PURSUIT.

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Introduction

Non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is a common emergency medical condition [1, 2]. Not only is the number of cases of this form of coronary heart disease (CHD) increasing, but patients also tend to get younger [3, 4].

Considering the variety of clinical variants that characterise the instability of the atherosclerotic plaque of the coronary arteries, analysing the prognosis of the development of fatal and non-fatal complications, both on the patient's admission to hospital and those delayed to occur within the first 30 days, is of particular importance. Special attention should be paid to the situation of NSTE-ACS without percutaneous coronary intervention (PCI).

In order to assess the development of short-term complications in patients with NSTE-ACS and to select the optimal scale, the results of comparative studies of the available risk prediction scales GRACE, TIMI, PURSUIT, RECORD, PREDICT are presented [5, 6]. However, the comparative effectiveness of these scales in patients with NSTE-ACS in the absence of PCI during emergency hospitalisation remains controversial, indicating the need for more in-depth study of this issue.

The aim of this study was to compare the short-term prognosis of fatal and non-fatal complications using GRACE (Global Registry of Acute Cardiac Events risk score), TIMI (Thrombolysis In Myocardial Infarction), PREDICT (PREdicting risk of Death In Cardiac Disease Tool), PURSUIT (Platelet Glycoprotein IIb-IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy) and RECORD in patients with non-PCI NSTE-ACS ST.

Methods

The patient sample was formed in 2 years (2017-2019) and consisted of 122 patients admitted to "Mordovian Republican Central Clinical Hospital" with the referral diagnosis "NSTE-ACS". The absence of primary PCI during the patient's hospitalisation is a unique feature of this sample. The study was in accordance with the standards of good clinical practice and the requirements of the Declaration of Helsinki. The study protocol was approved by the local ethics committee of the National Research Ogarev Mordovia State University on 17 June 2017 (protocol #40). All participants gave written informed consent to be examined before the study.

Non-inclusion criteria: acute coronary syndrome with ST-segment elevation, myocarditis, pericarditis, arrhythmias not related to NSTE-ACS.

Exclusion criteria: incomplete laboratory and instrumental data.

The mean age of the patients was 62.2 ± 8.9 years (min age 36 years, max age 83 years), including 35 fe-

males (28.6 %) and 87 males (71.4 %). The mean age of the women was older (65.3 ± 8.1 years) compared to the mean age of the men (61.7 ± 9.4 years).

According to electrocardiogram (ECG) data in the group of NSTE-ACS patients, ST-segment depression corresponding to subendocardial myocardial infarction (MI) was detected in 41 patients (33.6 %) and T inversion in 36 patients (29.5 %). A positive troponin test was obtained in 25 patients (20.5 %). The same group included 8 % of patients with recurrent MI. In addition, 36.9 % of patients were diagnosed with unstable angina.

9 (7.4 %) patients were admitted with a complicated course of NSTE-ACS: pulmonary oedema in 6 (4.9 %) patients and cardiogenic shock with due to atrial fibrillation (AF) paroxysms in 3 (2.5 %) patients. Rhythm disturbances were recorded in 22 patients: in 7 patients (5.7 %) the first diagnosis of AF was registered on the ECG, in 12 (9.8 %) patients a permanent form of AF was detected and in 3 (2.5 %) patients ventricular extrasystole of 4–5 Laun gradations.

Signs of chronic heart failure (CHF) stage II A — III were detected in 28 (22.9 %) patients (stage II A — 17 people (13.9 %), stage II B — 7 people (5.7 %), stage III — 4 people (3.3 %).

Comorbidities were common in NSTE-ACS patients: hypertension (AH) was present in 52 (42.6 %) patients and 31 (25.4 %) patients had compensated type 2 diabetes mellitus (DM).

Chronic kidney disease (CKD) with a glomerular filtration rate (GFR) below 40ml/min/1.73m^2 was found in 11 patients (9.0 %), 4 (3.2 %) patients had anaemia. No lung diseases such as bronchial asthma or chronic obstructive pulmonary disease were found in this group.

All patients at the pre-hospital stage and in the hospital were treated in accordance with the clinical protocol for the treatment of patients with STEMI of the Ministry of Health of the Russian Federation (2016) [7].

The absence of primary PCI was explained by refusal of coronary angiography (CAG) (age restrictions) in 14 (11.5 %) patients, and intolerance of contrast or anaesthetic in 8 (6.5 %) patients.

All the other 100 patients in this group underwent CAG. 27 (27 %) patients had intact coronary vessels, 42 (42 %) patients had a stenosis with severity of less than 50 %, and 31 (31 %) patients (all patients with type 2 DM) had a distal type of coronary stenosis.

The GRACE, TIMI, RECORD, PREDICT and PURSUIT scales were used to predict the risk of short-term complications in patients with NSTE-ACS without PCI.

The study design consisted of an initial assessment of the prognosis of fatal and non-fatal complications in patients with NSTE-ACS without PCI on hospital admission.

The study endpoint was then assessed 30 days after the admission. After the discharge, the development of complications (fatal and non-fatal) and repeat hospitalisations were assessed by outpatient clinic staff.

Statistical analysis

The results obtained were processed using the StatSoftStatistica 10.0 programme. For the assessment of the normality of the distribution of quantitative data Kolmogorov-Smirnov, Shapiro-Wilk criterions were used. Qualitative data are presented as relative indices (fractions, %). To analyse intergroup differences in quantitative characteristics, descriptive statistics were used with the Student's t-test and the Mann-Whitney rank U criterion, depending on the normality of the distribution. The χ^2 test, and Fisher's exact test when the number of observations was small, was used to identify differences in the frequencies of values of qualitative indicators between groups and to assess their statistical significance.

To assess the prognostic significance of the above-mentioned scales and their criteria, sensitivity (Se) and specificity (Sp) and relative risk (RR) with 95 % confidence interval (CI) were calculated.

The results were considered reliable at a significance level of $p < 0.05$.

Results

The analysis of the initial examinations and data from the short-term scales in NSTE-ACS patients without PCI showed an unclear distribution of the number of patients in relation to the degree of prognosis for complications (Table 1).

A high risk of complications was found in all five short-term scales, but the number of patients at this risk ranged from 1.6 % (PREDICT) to 36.9 % (TIMI).

The moderate risk of complications in NSTE-ACS patients without PCI was reported for the four scales, ranging from 23.8 % (PURSUIT) to 61.5 % (TIMI), except for the RECORD scale (where this risk level is

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Table 1. **Distribution of NSTE-ACS patients without PCI by risk stratification according to the scores of short-term prognostic scales**

Risk	GRACE, %	RECORD, %	PREDICT, %	TIMI, %	PURSUIT, %
High	20.5	18	1.6	36.9	7.4
Moderate	42.6	–	54.1	61.5	23.8
Low	36.9	82	44.3	1.6	68.8

Table 2. **Relationship of primary prognostic short-term scales to in-hospital mortality in NSTE-ACS patients without PCI**

Scales	Ratio	High risk		Moderate risk		Low risk	
		Assigned	Died	Assigned	Died	Assigned	Died
GRACE	absolute number n=	25	4	52	–	45	–
RECORD	absolute number n=	22	3	–	–	100	1
PREDICT	absolute number n=	2	1	66	3	54	–
TIMI	absolute number n=	45	4	75	–	2	–
PURSUIT	absolute number n=	9	2	29	1	84	1

not reported). Diametrically, the number of patients classified as low risk ranged from 1.6 % (TIMI) to 82 % (RECORD).

The development of fatal complications was only recorded on the first day of hospitalisation. During the two years of the study, 4 (3.3 %) NSTE-ACS patients without PCI died.

Given the presence of mortality in NSTE-ACS patients without PCI, we analysed the comparability of mortality and risk score as assessed by short-term prognostic scales at first admission (Table 2).

All 4 dead patients (100 %) were included in the high-risk category according to the GRACE and TIMI scales. However, the number of patients classified as high risk according to these scales is remarkable; according to the TIMI scale, there are 2 times more of these patients than according to the GRACE scale (45 patients and 25 patients, respectively).

Looking at the data on the risk distribution according to the RECORD scale, 3 patients (75 %) were included in the high-risk category and one patient was classified as being at low risk on admission.

Regarding the PURSUIT scale, two patients (50 %) were classified as high risk, with one patient classified as moderate and one as low risk.

On the PREDICT scale, as only two patients were in this category at the initial risk assessment for prognosis of complications, one patient (25 %) entered the high risk category. The remaining three patients were classified as moderate risk at the initial assessment.

Given the variation in the number of patients assigned to a particular risk category for fatal complications, sensitivity, specificity, and relative risk with 95 % CI were calculated to assess the prognostic significance of the above-mentioned scales (Table 3).

When determining the ratio of sensitivity and specificity for predicting fatal complications, the GRACE, TIMI and RECORD scales had higher prognostic values for this category of patients than the PREDICT and PURSUIT scales (Table 3).

Complications occurred in 16 patients (13.5 %) with NSTE-ACS without PCI during the hospitalisation and up to 30 days in the outpatient setting. Two patients (1.7 %) were hospitalised for the recurrent MI.

Table 3. **Comparative analysis of scales in sensitivity and specificity in patients with NSTE-ACS without PCI regarding the development of fatal complications**

Death	Se	Sp	RR (95 % CI)	X^2	p
GRACE	1.000	0.805	*	16.0461	0.0003
RECORD	0.750	0.839	13.636 (1.487-125.009)	9.07998	0.0025
PREDICT	0.250	0.992	20.00 (3.372-118.628)	15.9314	0.0003
PURSUIT	0.500	0.941	12.556 (1.997-78.953)	11.3423	0.0034
TIMI	1.00	0.695	*	7.07646	0.0290

Note. *RR was not calculated due to the absence of events in one of the groups.

Table 4. **Ratio of NSTE-ACS patients without PCI classified into risk groups for developing non-fatal complications**

Scales	Ratio	High risk		Moderate risk		Low risk	
		Assigned	Complications	Assigned	Complications	Assigned	Complications
GRACE	absolute number n=	21	8	52	7	45	1
RECORD	absolute number n=	19	4	–	–	99	12
PREDICT	absolute number n=	1	1	63	8	54	7
TIMI	absolute number n=	41	7	75	8	2	1
PURSUIT	absolute number n=	7	3	28	5	83	8

The paroxysmal form of AF was observed in 4 (3.4 %) patients. Early postinfarction angina manifested in 5 (4.2 %) patients and episodes of cardiac asthma due to hypertensive crisis were also recorded in 5 (4.2 %) patients.

A comparative analysis of patients with non-fatal complications and risk classification at initial hospital assessment was performed, taking into account the development of non-fatal complications in this group of patients during the first 30 days and including patients who died (Table 4). There were significant discrepancies in the number of patients with non-fatal complications and the risk categories obtained at the initial assessment of prognosis.

For example, according to the PREDICT scale, only one patient was at high risk of complications, while the rest were at moderate and low risk (see Table 4). According to the RECORD scale, out of 16 patients with non-fatal complications, 4 patients had a high risk of complications and 12 patients had a low risk. The GRACE (8 patients) and TIMI (7 patients) scales had the highest number of patients with a high risk of non-fatal complications, but at the same time up to 50 % of patients had a moderate risk of complications according to these scales.

We analysed the sensitivity and specificity of the presented scales in determining the prognosis of non-fatal complications in NSTE-ACS patients without PCI (Table 5), taking into account the revealed discrepancies between the number of patients classified in the complication prognosis categories and the number of patients who developed complications.

When determining the ratio of the sensitivity and specificity values of the short-term scales in relation to the prognosis of non-fatal complications in NSTE-ACS patients without PCI, the data obtained from the RECORD and TIMI scales did not reach the criterion of reliability. The PURSUIT and PREDICT scales showed high specificity but low sensitivity for the development of non-fatal complications in this group of patients. Only the GRACE scale showed high values of sensitivity and specificity regarding the prognosis of non-fatal complications in NSTE-ACS patients without PCI, compared to other scales studied.

Taking into account the obtained data of sensitivity and specificity of the short-term scales used in this study regarding the development of fatal and non-fatal complications, it is possible to use a unified scale for short-term prognosis in NSTE-ACS patients without PCI for the practical work of a physician. For this purpose, the ratio of all patients with complications to those with initial risk stratification was assessed (Table 6).

When analysing the distribution of NSTE-ACS patients without PCI, the majority of patients who developed complications, regardless of the outcome, were in the high-risk category according to the GRACE (60 %) and TIMI (55 %) prognostic scales. The lowest number of patients who developed complications were classified in the primary prognosis of complication development according to the PURSUIT (25 %) and PREDICT (10 %) scales.

According to the RECORD scale, 35 % of patients who experienced complications of varying severity were classified in the high-risk category.

Table 5. **Comparative analysis of scales in sensitivity and specificity in patients with NSTE-ACS without PCI regarding the development of non-fatal complications**

Complications	Se	Sp	RR (95% CI)	X^2	p
GRACE	0.500	0.851	6.059 (3.113-11.792)	15.6084	0.0004
RECORD	0.250	0.851	1.719 (0.620-4.765)	1.04581	0.3064
PREDICT	0.063	1.000	7.733 (4.823-12.401)	6.37324	0.0413
TIMI	0.438	0.663	1.442 (0.579-3.588)	3.15078	0.2069
PURSUIT	0.188	0.960	3.626 (1.339-9.820)	6.53129	0.0381

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Table 6. **Ratio of NSTE-ACS patients without PCI matched by risk group regarding the development of fatal and non-fatal complications**

Scales	Ratio	High risk		Moderate risk		Low risk	
		Assigned	Any compications	Assigned	Any compications	Assigned	Any compications
GRACE	absolute number n=	25	12	52	7	45	1
RECORD	absolute number n=	22	7	–	–	100	13
PREDICT	absolute number n=	2	2	66	11	54	7
TIMI	absolute number n=	45	11	75	8	2	1
PURSUIT	absolute number n=	9	5	29	6	84	9

Table 7. **Comparative analysis of scales in terms of sensitivity and specificity in patients with NSTE-ACS without PCI in the development of complications regardless of outcome**

Complications	Se	Sp	RR (95 % CI)	X^2	p
GRACE	0.600	0.873	5.820 (2.670-12.685)	22.918	<0.001
RECORD	0.350	0.853	2.448 (1.106-5.417)	4.659	0.031
PREDICT	0.100	1.000	6.667 (4.354-10.207)	10.370	0.002
TIMI	0.550	0.667	2.091 (0.939-4.657)	3.372	0.067
PURSUIT	0.250	0.961	4.185 (1.976-8.866)	10.873	<0.001

Considering the search for the most informative short-term scale for the purpose of risk stratification regardless of the outcome of complication development in NSTE-ACS patients without PCI, a comparative analysis of the scales was performed according to the criteria of sensitivity and specificity (Table 7).

The values of the TIMI scale obtained in this study did not meet the criterion of validity in terms of sensitivity and specificity for the development of all categories of complications in patients with NSTE-ACS without PCI. The RECORD, PREDICT and PURSUIT scales generally have high specificity but low sensitivity. In patients with NSTE-ACS without PCI, the GRACE scale was the most informative scale for prognosis of complications regardless of outcome.

Discussion

All of the short-term scales presented in this study have an evidence base for their ability to predict complications in patients with ACS [8]. However, it should be taken into account that the algorithms of these scales were developed in the context of heterogeneous clinical situations with heterogeneous medical approaches and patients belonging to different ethnic groups.

Scales such as GRACE, RECORD and PREDICT have been developed and proposed for ACS situations regardless of ST segment changes and have a single set of values. TIMI scale is also developed and proposed for ACS with and without ST elevation, but has two variants of set of values specifically for each ACS situation. The prognostic value of these scales lies in the assessment of the risk of death, mortality and the development of MI. Only the PURSUIT scale estimates the risk of death, MI in NSTE-ACS patients for the period of monthly follow-up in patients without PCI [9].

There is insufficient information in the literature to compare the short-term prognostic scales GRACE, RECORD, PREDICT, TIMI and PURSUIT in NSTE-ACS without PCI.

However, in routine clinical practice, it is necessary to have a unified scale for risk stratification of the development of short-term complications, which will allow a quicker decision on treatment, due to the daily need of the physician to make a decision on the tactics of patient management.

In our study, we are particularly interested in the prognostic significance of the TIMI and PURSUIT scales, which have a specific set of markers for NSTE-ACS patients.

Regarding the TIMI scale, Antman E. M. et al. developed a comprehensive approach to determine the risk of death, MI, recurrent angina and/or the need for urgent revascularisation in patients with NSTE-ACS.

In our study of NSTE-ACS and non-PCI patients, this model showed high sensitivity and specificity only for the prediction of fatal complications (Se = 1.00 Sp = 0.695 at $X^2 = 7.07646$, p = 0.0290) in contrast to the prediction of non-fatal complications (Se = 0.438 Sp = 0.663 95 % CI = 1.442 (0.579–3.588) at $X^2 = 3.15078$, p = 0.2069). Similarly, this model did not demonstrate reliability in predicting short-

term complications as a function of outcome (Se = 0.550 Sp = 0.667 95 % CI = 2.091 (0.939-4.657) X^2 = 3.372, p = 0.067).

The prognostic significance of the short-term PURSUIT scale is based on Platelet Glycoprotein IIb-IIIa in unstable angina: Receptor Suppression Using Integrilin Therapy study. It assesses the risk of death and MI in NSTE-ACS patients over a one-month follow-up period in patients without PCI.

In our study of NSTE-ACS patients without PCI, we did not find a superior prognostic performance of this scale compared to other short-term scales studied. Both in the prediction of fatal complications (Se = 0.500 Sp = 0.941 95 % CI = 12.556 (1.997–78.953) X^2 = 11.3423 at p = 0.0034) and non-fatal complications (Se = 0.188 Sp = 0.960 95 % CI = 3.626 (1.339 – 9.820) X^2 = 6.53129 at p = 0.0381), and in predicting complications independent of outcome (Se = 0.250 Sp = 0.961 95 % CI = 4.185 (1.976-8.866) X^2 = 10.873 at p < 0.001) showed not only high specificity but also low sensitivity.

The PREDICT scale was proposed as a risk stratification for short-term prognosis after hospitalisation for ACS (acute MI and unstable angina).

The analysis of the prognostic efficacy with regard to the development of complications in NSTE-ACS patients without PCI showed that this scale had not only a high specificity but also a low sensitivity in all three risk assessment categories, regardless of the outcome of the complications development. Fatal complications (Se = 0.250 Sp = 0.992 95 % CI = 20.00 (3.372-118.628) X^2 = 15.9314 at p = 0.0003); non-fatal complications (Se = 0.063 Sp = 1.000 95 % CI = 7.733 (4.823-12.401) X^2 = 6. 37324 at p = 0.0413); when assessing the development of complications regardless of outcome (Se = 0.100 Sp = 1.000 95 % CI = 6.667 (4.354–10.207) X^2 = 10.370 at p = 0.002).

In order to create the RECORD prognostic scale, the ACS registry was created in domestic hospitals, which suggests its relevance for the Russian population and characterises its prognostic efficacy in relation to the development of mortality and MI in the hospital period.

In the study carried out, the RECORD scale showed high values of sensitivity and specificity while determinating the prognosis of fatal complications (Se = 0.750 Sp = 0.839 95 % CI = 13.636 (1.487–125.009) X^2 = 9.07998 with p = 0.0025), surpassing the ability to predict non-fatal complications (Se = 0.250 Sp = 0.851 95 % CI = 1.719 (0.620–4.765) X^2 = 1.04581 with p = 0.3064) and to predict any complications (Se = 0.350 Sp = 0.853 95 % CI = 2.448 (1.106-5.417) X^2 = 4.659 with p = 0.031).

A comparative analysis of the GRACE scale in predicting short-term complications in patients with NSTE-ACS without PCI showed high sensitivity and specificity in predicting the development of fatal (Se = 1.000 Sp = 0.805 95 % CI = X^2 = 16.0461 at p = 0.0003) and non-fatal (Se = 0. 500 Sp = 0.851 95 % CI = 6.059 (3.113–11.792) X^2 = 15.6084 at p = 0.0004) complications, and in predicting complications regardless of outcome (Se = 0.600 Sp = 0.873 95 % CI = 5.820 (2.670–12.685) X^2 = 22.918 at p < 0.001), compared to all other scales examined in this study.

Conclusion

Thus, in NSTE-ACS patients without PCI, only the GRACE scale showed higher sensitivity and specificity than the short-term scales used in this study (RECORD, PREDICT, TIMI and PURSUIT), when comparing the ability to predict the short-term fatal and non-fatal complications, as well as any type of adverse outcomes. At the same time, scales such as TIMI and RECORD showed significantly higher values of sensitivity and specificity in predicting the development of fatal complications in this category of patients compared to the PREDICT and PURSUIT scales.

Conflict of interest: none declared.

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