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The influence of the Initial Severity of Coronary Artery Lesion (by the Syntax Score) on the Midterm Prognosis of Patients With Acute Myocardial Infarction Without ST Segment Elevation

Aim — To study the effect of the baseline severity of coronary artery damage according to the SYNTAX scale (baseline score of coronary lesions, BSCL) on the mid-term prognosis in patients with non-ST segment elevation acute myocardial infarction (AMI) (NSTEMI), and to identify the threshold BSCL value that determines high and low risks of adverse cardiac outcomes.

Material and Methods — A retrospective analysis was performed for the hospital treatment of patients with NSTEMI (n=421) who had undergone percutaneous coronary intervention (PCI). 256 patients with a repeated hospitalization in mid-term (11.6±3.2 months) were selected for the study. These patients were followed up for the incidence of acute coronary syndrome (ACS), unscheduled repeated myocardial revascularization (URR), and of the composite endpoint (CEP) that included at least one the following events: death, recurrent AMI, unstable angina (UA), and URR. The effect of BSCL on the incidence of these events in mid-term was proven ($p<0.05$), and then the BSCL threshold value was determined, which allowed segregation of patients into groups of high and low risk of adverse cardiac outcomes.

Results — The threshold BSCL value for the risk of ACS was determined as score 14 (odds ratio, OR, 2.79; 95% confidence interval, CI: 1.32–5.89); for URR and CEP, score 13 (OR, 2.21; 95% CI: 1.22–4.01 and OR, 2.38; 95% CI: 1.32–4.31, respectively). Since these threshold values were comparable, for the composite category of events (CEP), the BSCL threshold comprised score 13, and namely this value was taken as a base. According to the multifactorial Cox regression at BSCL score ≥13, the probability of earlier CEP in mid-term was 2.44 times higher than at lower BSCL values (OR, 2.44; 95% CI: 1.41–4.21; p=0.001). Furthermore, according to the Kaplan-Meier estimate, the effect of BSCL on the survival without adverse cardiac outcomes becomes significant starting from the second half-year (p=0.001, log-rank test).

Conclusion — In NSTEMI patients, the SYNTAX baseline score of coronary lesions >13 is an independent predictor of adverse cardiac outcomes in mid-term starting from the second half-year. Thus, patients with BSCL ≥13 should undergo a follow-up examination no later than at 6 months independent on their clinical condition.

Keywords — Non-ST segment elevation acute myocardial infarction; SYNTAX scale; percutaneous coronary intervention; mid-term prognosis

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Increasing attention is given every year to studying acute non-ST-segment elevation myocardial infarction (NSTEMI). This is due to the high prevalence of this pathology (about two thirds of all cases of acute myocardial infarction (AMI) [1–3]) and adverse long-term prognosis. The hospital mortality is lower in patients with NSTEMI than in patients with acute ST-segment elevation myocardial infarction (STEMI) [3, 4], however, three years later, it is on average 2 times higher for NSTEMI [2, 5].

A number of studies showed that the main reason for such an adverse prognosis is that patients with NSTEMI are older, have comorbidities and multivessel coronary artery disease more often [3, 6]. This makes it difficult to select management strategy during and after hospital treatment of patients of this group. Objective stratification of the risk of complications is obviously required to improve outcomes. Clear differentiation of high-risk and low-risk patients will make it possible to select the most rational treatment and prevention algorithms.

There is no ideal score for stratifying the risk of complications [7, 8]. The prognostic role of the angiographic SYNTAX score has been actively studied recently in various populations of patients with CAD [9–12]. It has been shown that the higher the initial severity of coronary artery involvement according to the SYNTAX score, the greater the probability of adverse cardiac outcomes [9–12]. There is no so far baseline coronary artery involvement index (BCAII) cut-off values that differentiate between high risk and low risk of complications. Accordingly, BCAII cut-off values vary from 8 to 36 in the literature [9–12]. It is important to note that this issue has not been investigated in patients with NSTEMI.

Thus, with the high incidence of multivessel coronary artery disease in patients with NSTEMI (60–70%) [3, 6], it is necessary to study the prognostic value of BCAII and determine its cut-off value in order to objectify the management of this group of patients.

Objective

Study the effect of the baseline severity of coronary artery involvement (SYNTAX score) on the mid-term prognosis for patients with NSTEMI and determine the cut-off value of BCAII that divide patients into the groups of high risk and low risk of adverse cardiac outcomes.

Material and Methods

The study was performed following of the Declaration of Helsinki. A retrospective analysis of inpatient treatment of 421 patients with NSTEMI was conducted. Elevated markers of myocardial damage and percutaneous coronary intervention (PCI) were the inclusion criteria. Subjects with postinfarction cardiosclerosis, a history of myocardial revascularization, and severe comorbidities were excluded.

Selective coronary angiography was performed using the Judkins method. The severity of baseline coronary artery involvement was assessed using the SYNTAX score. Coronary artery stenosis ≥70% was considered hemodynamically significant, and ≥50% in the case of involvement of the left coronary artery with a diameter of ≥1.5 mm [3].

In the post-hospital period (11.6 ± 3.2 months), patients were re-admitted emergently with the diagnosis of ACS and electively with stable forms of CAD or for control coronary artery angiography about 6 months after PCI, which was the standard recommendation at discharge for all patients with NSTEMI even if they did not have complaints and clinical symptoms.

The findings of the first stage were published earlier [13]: it was shown that BCAII influenced the clinical status of patients with NSTEMI before PCI and its cut-off values were established.

The influence of BCAII on the mid-term prognosis was studied in the second stage described in this publication. For this purpose, 256 patients were selected from the general group of patients with NSTEMI, who were re-hospitalized on average after 11.6 ± 3.2 months. During the study period, the incidence of ACS, emergency repeat revascularization (ERR), and composite endpoint (CEP), including at least either death, recurrent AMI, unstable angina (UA), and ERR, were evaluated. Statistically significant effect of BCAII on the incidence of mid-term adverse cardiac outcomes was initially established. Cut-off values of BCAII for the high risk of each separate event and CEP were defined subsequently. Patients were divided into groups depending on the established cut-off values.

Statistical analysis

The data obtained were processed using IBM SPSS Statistics 26.0. The quantitative data are presented as the means (M) and standard deviations (SD) or the medians (Me) and interquartile ranges ([Q1; Q3]). The categorical characteristics are expressed as the absolute numbers (n) and percentages (%). The Student's t-test or Mann-Whitney U-tests were used to compare two independent groups by quantitative indicators depending on the type of variable distribution. The Pearson's chi-square test/Fisher's exact test and odds ratio (OR) with 95% confidence interval (CI) were used in the qualitative comparisons. ROC analysis was used to determine the cut-off values for BCAII. Multivariate Cox regression was used to assess the effect of BCAII on the development of mid-term adverse cardiac outcomes. The p-value < 0.05 was used as the level of statistical significance.

Results

In the mid-term period, 62 (24.2%) of the 256 re-admitted patients had CEP. ACS was reported in 35 (13.7%) patients, of whom 28 (10.9%) had UA, and 7 (2.8%) patients had recurrent AMI. 2 (0.8%) patients died of complications of recurrent AMI during hospitalization. 60 (23.4%) patients were subjected to myocardial ERR.

In the course of studying the effect of BCAII on the mid-term prognosis, this indicator was found to be statistically significantly higher in ACS, ERR, and CEP than in the absence of these events (Table 1).

A ROC analysis was performed for ACS, ERR, and CEP to determine BCAII cut-off values that can be used to divide patients into the groups of high risk and low risk for these outcomes during the study period.

Figure 1 shows the ROC curve characterizing the dependence of the ACS risk on BCAII (AUC 0.62±0.05; 95% CI 0.51–0.72; p=0.029). BCAII cut-off value was 14 (sensitivity 62.9%, specificity 61.1%).

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Table 1. Comparison of BCAIIs based on the presence of mid-term adverse cardiac outcomes

Outcome	BCAII (Me [Q1; Q3])		p
	presence of outcome	absence of outcome	
ACS (n = 35;13.7 %)	19 [10; 24.5]	12 [9; 19]	0.028
ERMR (n = 60;23.4 %)	17.5 [10; 23]	11 [9; 19]	0.029
CEP (n = 62;24.2 %)	17.5 [10; 23]	11 [9; 19]	0.017

BCAII, baseline coronary artery involvement index; ACS, acute coronary syndrome; ERMR, emergency repeat myocardial revascularization; CEP, composite endpoint.

The odds for the onset of ACS with BCAII ≥14 were 2.79 times higher than with lower values of the index (OR 2.79; 95% CI 1.32–5.89).

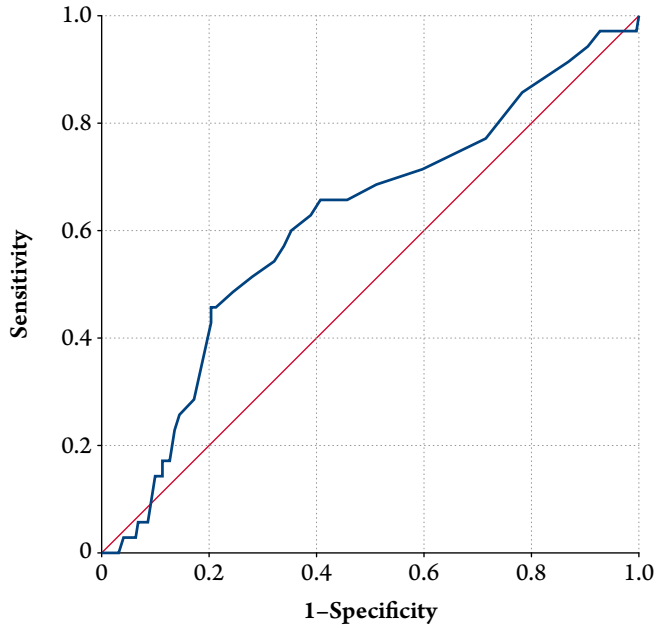
In the ROC analysis characterizing the dependence of the risk of ERR on BCAII (Figure 2), AUC was 0.59±0.04 (95% CI 0.51–0.68; p=0.029). BCAII cut-off value was 13 (sensitivity 60.0%, specificity 60.7%). The odds for ERR with BCAII ≥ 13 were 2.21 times higher than with lower values of the index (OR 2.21; 95% CI 1.22–4.01).

For the odds of ERR, the cut-off value of BCAII was 13 (sensitivity 61.3%, specificity 62.3%). AUC was 0.60±0.04 (95% CI 0.52–0.68; p=0.017; Figure 3). The odds for the onset CEP with BCAII ≥ 13 were 2.38 times higher than with BCAII < 13 (OR 2.38; 95% CI 1.32–4.31).

Given that the established cut-off values of BCAII (13 and 14) are comparable and that BCAII threshold was 13 for the composite category of events (CEP), this value was taken as a basis.

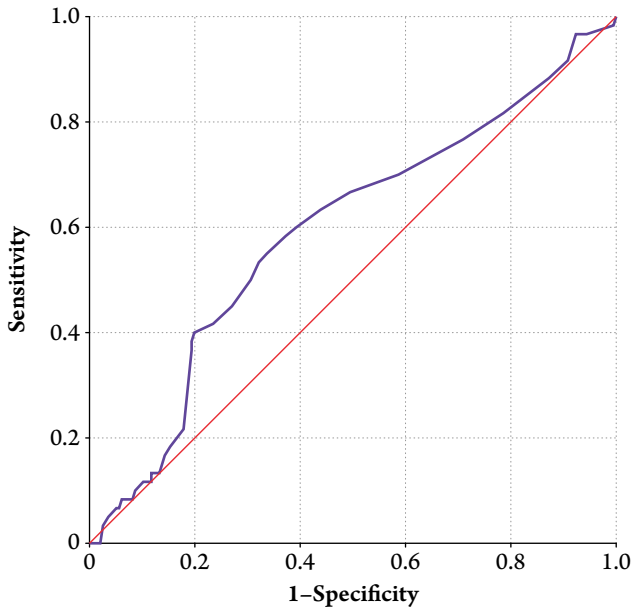
Multivariate Cox regression analysis was conducted to determine the prognostic value of the BCAII cut-off (13) taking into consideration its interaction with other factors that can affect the post-hospital period (Table 2). CEP was used as the outcome, and the suggested predictors were: BCAII ≥13, age (as a continuous

Figure 1. ROC-curve characterizing the dependence of ACS risk on BCAII



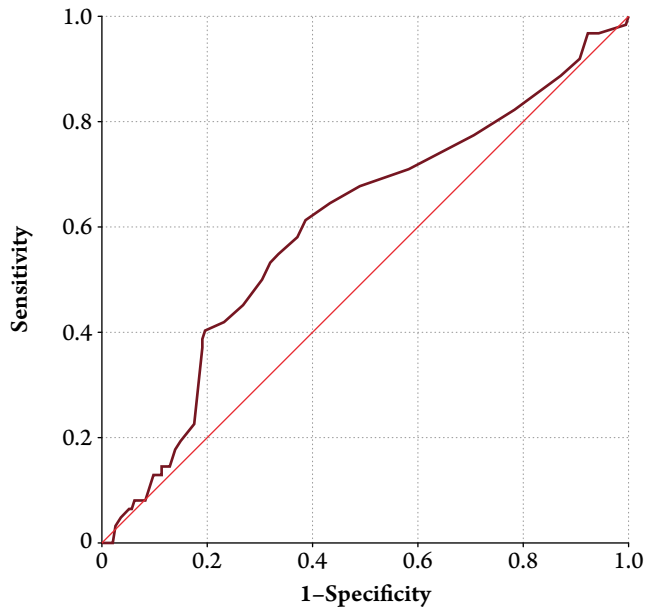
BCAII, baseline coronary artery involvement index.

Figure 2. ROC-curve characterizing the dependence of ERMR risk on BCAII



BCAII, baseline coronary artery involvement index; ERMR, emergency repeat myocardial revascularization.

Figure 3. ROC-curve characterizing the dependence of CEP risk on BCAII



BCAII, baseline coronary artery involvement index; CEP, composite endpoint.

Table 2. Results of the Cox regression analysis to assess predictors of CEP during the study period

Parameter	Univariate Cox analysis			Multivariate Cox analysis		
	HR	95 %CI	p	HR	95 %CI	p
BCAII ≥13	2.69	1.59–4.57	< 0.001	2.44	1.41–4.21	0.001
Age, years	1.03	1.002–1.06	0.037	1.02	0.99–1.05	0.203
Absence of statin therapy	1.66	1.003–2.75	0.049	1.68	1.01–2.78	0.044

CEP, composite endpoint; HR, hazard ratio; CI, confidence interval; BCAII, baseline coronary artery involvement index.

variable rather than a specific range), male sex, family history of cardiovascular diseases, arterial hypertension, diabetes mellitus, obesity, smoking, total cholesterol (as a continuous variable rather than a specific range) at re-admission, and non-use of acetylsalicylic acid, clopidogrel, and statins in the post-hospital period. Consequently, a statistically significant proportional hazard model was created (chi-square 18.47; p<0.001), with BCA ≥13 (hazard ratio (HR) 2.44; 95% CI: 1.41–4.21; p=0.001) and non-use of statins (OR 1.68; 95% CI: 1.01–2.78; p=0.044) as the independent predictors for the onset of CEP in the mid-term period. Thus, the probability of an earlier onset of CEP in the mid-term period was 2.44 times higher in patients with BCAII ≥13 than in patients with BCAII <13 (p = 0.001).

The Kaplan-Meier analysis (Figure 4) showed that BCAII did not significantly affect survival without adverse cardiac outcomes in the first six months (p=0.345, log-rank test). However, the differences became statistically significant by the end of 12 months: the percentage of patients with BCAII <13 and without CEP was 92.8%, and with BCAII ≥13–76.6% (p=0.001, log-rank test). The difference of more than 30% was observed after 15 months (84.4% and 52.6%; p<0.001, log-rank test).

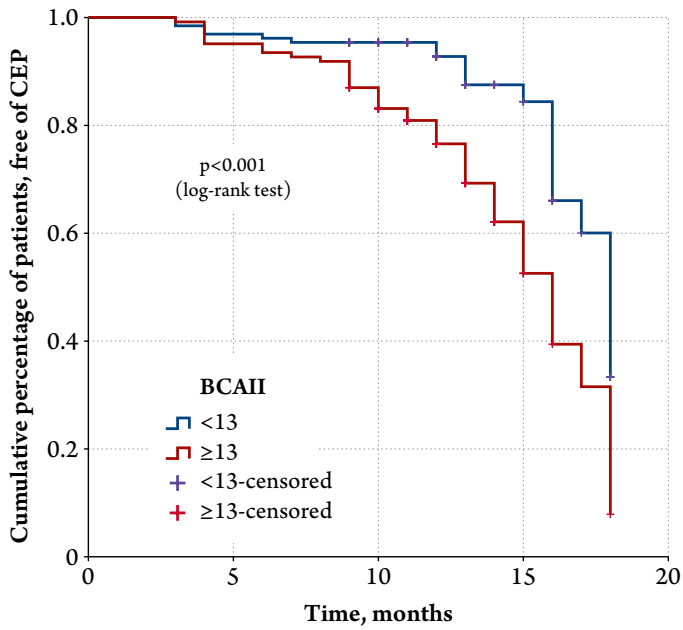
Thus, we have shown that BCAII ≥13 is an independent predictor of adverse cardiac outcomes in patients with NSTEMI in the mid-term period. On that basis, the patients were divided into two groups: Group 1 with BCAII <13 (n=132) and Group 2 with BCAII ≥13 (n=124).

There were some differences in the baseline clinical and anamnestic characteristics (Table 3).

Given the principle of patient grouping, it is obvious that Group 2 differed from Group 1 by greater baseline severity of coronary artery involvement (Table 4). It should be noted that the frequency of bare metal stent placement into an infarct-related artery (IRA) was comparable: 28.8% in Group 1 and 31.5% in Group 2 (p=0.642). Complete myocardial revascularization was conducted in 81.8% of cases in Group 1 and only in 36.3% in Group 2 (p<0.001).

Coronary angiography showed that the mid-term frequency of IRA restenosis was comparable in the groups, 16.7% (n = 22) and 16.9% (n = 21), respectively (p=0.954).

Figure 4. Kaplan-Meier curves for predicting CEP risk in patients with BCAII < 13 and BCAII ≥13



BCAII, baseline coronary artery involvement index; CEP, composite endpoint.

At the hospital stage, drug therapy differed only in the administration of nitrates, which were prescribed in Group 2 more often (39.5% and 16.7%, respectively; p<0.001), which is quite natural given the higher incidence of incomplete revascularization. In the post-hospital period, the percentages of patients taking clopidogrel and statins were comparable (p > 0.05). In Group 2, however, patients took acetylsalicylic acid more often (79.0% and 62.9%, respectively; p=0.005).

Discussion

Despite rapid advances in CAD treatment, patients with NSTEMI still have adverse mid-term and long-term prognosis [2, 3]. In most cases, they do not have clinically significant complications in hospital, which often results in the underestimation of the risk of possible adverse cardiac outcomes in the future [8]. Therefore, it is of utmost importance to find criteria for maximum objectification of the prognosis in patients with NSTEMI. We used the angiographic SYNTAX score for the risk stratification [9–12].

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Table 3. Baseline clinical and anamnestic characteristics of patients with BCAII < 13 and BCAII ≥ 13

Parameter	Group 1, BCAII < 13 (n = 132)	Group 2, BCAII ≥ 13 (n = 124)	p
Age, years (M ± SD)	56 ± 9.1	63 ± 10.1	< 0.001
Male, n (%)	100 (75.8)	81 (65.3)	0.067
Significant family history of cardiovascular diseases, n (%)	46 (34.8)	40 (32.3)	0.661
Arterial hypertension, n (%)	102 (77.3)	104 (83.9)	0.183
Smoking, n (%)	69 (52.3)	47 (37.9)	0.021
Diabetes mellitus, n (%)	19 (14.4)	25 (20.2)	0.222
Chronic kidney disease, n (%)	15 (11.4)	9 (7.3)	0.362
GRACE >140, n (%)	31 (23.5)	49 (39.5)	0.006
Creatine kinase MB, mmol/L, (Me [Q1; Q3])	41.0 [32.0; 59.5]	69.5 [42.0; 105.5]	< 0.001
ST-segment depression ≥ 1.0 mm, n (%)	74 (56.1)	85 (68.5)	0.040
Left ventricular ejection fraction ≤ 45%, n (%)	9 (6.8)	21 (16.9)	0.012

BCAII, baseline coronary artery involvement index.

We were able to show that the baseline severity of coronary artery involvement affected the incidence of mid-term adverse cardiac outcomes in patients with NSTEMI. This dependence had been identified earlier in different CAD populations [9–12]. However, specific cut-off values of BCAII were determined in the proposed study for the first time, which allowed dividing patients with NSTEMI into groups of high risk and low risk of complications. Cut-off BCAII was 14 for ACS (OR 2.79; 95% CI 1.32–5.89) and 13 for ERR and CEP (OR 2.21; 95% CI 1.22–4.01 and OR 2.38; 95% CI 1.32–4.31, respectively). Multivariate Cox regression analysis showed that BCAII ≥ 13 was an independent predictor of CEP onset (HR 2.44; 95% CI 1.41–4.21; p=0.001) in the mid-term period. Even with the correction for interaction with other factors, the risk of earlier onset of CEP is 2.44 times higher in patients with BCAII ≥ 13 than in patients with BCAII <13.

It should be noted that we used a mathematical approach (ROC-analysis) to determine the cut-off value of BCAII, while it was selected empirically in most publications, that is, blindly, and its predictive significance was verified subsequently [10, 11]. In one of the few relevant studies in patients with NSTEMI, in which ROC-analysis was also used, the BCAII cut-off values of 10–13 were established [9], which is comparable with our findings (13 and 14), but their prognostic value was relatively lower. In our study, AUC for ERR was 0.59 (95% CI 0.51–0.68), while in the study by Palmerini et al. [9], it was 0.56 (95% CI 0.52–0.59), and CEP AUC was 0.60 (95% CI 0.52–0.68) and 0.57 (95% CI 0.54–0.60), respectively. These discrepancies may be due to different approaches to calculating

Table 4. Angiographic characteristics of patients with BCAII < 13 and BCAII ≥ 13

Parameter	Group 1, BCAII <13 (n = 132)	Group 2, BCAII ≥13 (n = 124)	p
BCAII (Me [Q1; Q3])	9 [8; 11]	21 [17; 28]	< 0.001
Right coronary circulation, n (%)	126 [95.5]	49 [94.4]	0.908
IRA:			
• LCA trunk, n (%)	0	7 (5.6)	0.006
• Left anterior descending artery, n (%)	83 (62.9)	61 (49.2)	0.028
• Left circumflex artery, n (%)	22 (16.6)	30 (24.2)	0.135
• Right coronary artery, n (%)	27 (20.5)	26 (21.0)	0.920
Multivessel coronary artery disease, n (%)	59 (44.7)	110 (88.7)	< 0.001
IRA occlusion, n (%)	7 (5.3)	41 (33.1)	< 0.001
Chronic coronary artery occlusion, n (%)	3 (2.3)	20 (16.1)	< 0.001
Complete myocardial revascularization, n (%)	108 (81.8)	45 (36.3)	< 0.001
Stenting of ≥ 2 coronary arteries, n (%)	32 (24.2)	46 (37.1)	0.026
Bare-metal stent in IRA, n (%)	38 (28.8)	39 (31.5)	0.642

BCAII, baseline coronary artery involvement index; IRA, infarct-related artery.

the severity of coronary artery involvement. Stenosis > 50% was taken into consideration by Palmerini et al. [9], and we considered stenosis > 70%. Our choice was justified by the fact that ≥ 70% narrowing is considered in clinical practice to be hemodynamically significant and requiring revascularization.

The prognosis using the Kaplan-Meier prognosis method showed survival without adverse cardiac outcomes in the first 6 months does not depend on BCAII (p=0.345, log-rank test). However, the differences became statistically significant by the end of 12 months: the percentage of patients without CEP with BCAII <13 was 92.8%, and with BCAII ≥13–76.6% (p = 0.001, log-rank test). Therefore, it is advisable to recommend a repeat cardiac examination to patients with BCAII ≥13 not later than after 6 months, even in the absence of complaints and clinical symptoms.

Limitations

The study was limited by the retrospective and single-center design. However, it should be noted that high representativeness of the sample and the use of modern, generally accepted statistical methods allow obtaining reliable results.

The analysis of the resulting data showed statistically significant differences in the frequency of complete myocardial revascularization in the study groups (81.8% in Group 1 and 36.3% in Group 2; p < 0.001). In our previous article, the effect of the revascularization completeness according to the SYNTAX score (residual coronary artery involvement index (RCAII)) on the mid-term prognosis was shown in patients with NSTEMI [14]. Accordingly, it should be concluded that both BCAII and RCAII are predictors of adverse cardiac outcomes. This is expected considering the statistically significant direct correlation between these indicators, which we have identified earlier (r=0.604; p<0.001) [14], and consistently with the literature data [3]. Obviously, the completeness of myocardial revascularization depends largely on the baseline severity of coronary artery involvement. At the same time, the comparison results of the ROC-analysis data showed the superiority of RCAII over BCAII in predicting the risk of death and/or ACS in patients with NSTEMI in the mid-term period (AUC 0.71±0.05 and 0.62±0.05, respectively) [14]. Nevertheless, in our opinion, it is reasonable to use both SYNTAX indicators in clinical practice to stratify the risk of complications in order to determine the optimal strategy of PCI and post-hospital management of patients with NSTEMI.

Conclusion

Baseline severity of initial coronary artery involvement of SYNTAX ≥13 in patients with myocardial infarction without ST-segment elevation is an independent predictor of adverse cardiac outcomes in the mid-term period starting from the second 6 months. Therefore, it is advisable to recommend a repeat cardiac examination to patients with baseline coronary artery involvement index ≥13 not later than after 6 months, even in the absence of complaints and clinical symptoms.

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