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PROGNOSTIC VALUE OF RESIDUAL CORONARY ARTERY LESIONS ON THE SYNTAX SCALE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION WITHOUT ST SEGMENT ELEVATION IN THE MID-TERM PERIOD

<i>Aim</i>	To study the effect of residual coronary injury after a percutaneous coronary intervention (PCI), as evaluated with the SYNTAX scale (residual SYNTAX score, RSS), on the mid-term prognosis for patients with non-ST elevation acute myocardial infarction (NSTEMI) and also to determine threshold RSS values for patients at high and low risk of adverse cardiac events.
<i>Material and methods</i>	A single-center, retrospective study was performed. From 421 patients with NSTEMI after PCI with stenting, 169 patients were selected who originally had multivessel coronary disease and who had undergone a repeated inpatient examination, including mid-term (11.7±3.0 mos.) coronary angiography. The endpoints were recurrent clinical manifestations of angina, repeat revascularization (RR), unstable angina (UA), recurrent acute myocardial infarction (AMI), cardiac death, and also a composite endpoint (major adverse cardiac events, MACE) that included UA, recurrent AMI, and cardiac death. After revealing a significant direct correlation between RSS and the probability of recurrent AMI, UA, MACE, or RR ($p<0.05$) using the ROC analysis, we have established threshold RSS values that divided patients into groups with high and low risk of the cardiac events listed above.
<i>Results</i>	For a significantly high risk of recurrent AMI (area under the curve, AUC 0.79±0.05; 95% confidence interval, CI 0.68–0.89; $p=0.048$), the threshold RSS score was 8 (sensitivity 100%, specificity 70.9%). For UA and MACE, the RSS scores were both 3 (AUC 0.68±0.5; 95% CI 0.58–0.79; $p=0.005$ and AUC 0.71±0.05; 95% CI 0.61–0.8; $p=0.001$, respectively). The probability of UA during the observation period with RSS >3 was 4.07 times higher and that of MACE was 5.23 times higher than with RSS <3 (95% CI 1.44–11.49; $p=0.01$ and 95% CI 1.88–14.53; $p=0.001$, respectively).
<i>Conclusion</i>	The study demonstrated a significant, direct correlation between the RSS and the risk of adverse cardiac events in patients with NSTEMI during one year of observation. Specific threshold values were obtained, which may help in choosing both the extent of revascularization and the tactics for postoperative management of patients.
<i>Keywords</i>	Non-ST elevation acute myocardial infarction, residual SYNTAX score, percutaneous coronary intervention, MACE, repeat revascularization, mid-term prognosis
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In recent times researchers have focused not only on improving the immediate outcomes of percutaneous coronary intervention (PCI) in various forms of acute coronary syndrome (ACS), but also on identifying the objective indicators which determine long-term prognosis, in order to improve patient management strategy [1]. The SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) score is currently the most commonly used instrument to stratify the risk of complications [2–7].

Although it has long been proven that the completeness of revascularization largely determines long-term

prognosis [6, 8], in real-world clinical practice complete correction is not always possible [4]. Therefore, the concept being actively developed today is so-called ‘reasonable’ incomplete revascularization [3] which minimizes the probability of an unfavorable outcome. A search is underway for the threshold value of residual SYNTAX score (RSS) showing residual coronary artery disease after PCI, which would make it possible to distinguish between patients with a high and low risk of long-term cardiac complications. However, due to the heterogeneity of the observational data and different approaches even to the very concept of hemodynamically

significant coronary stenosis (>50% or >70%), there is still no exact, objectively substantiated threshold value of RSS. The literature provides the threshold RSS values from 2 to 15 [2, 3, 5–7].

Non-ST-segment elevation acute myocardial infarction (NSTEMI-AMI) is a particular form of ACS, since it accounts for the majority of all AMI cases (about 70%) [9]. Its long-term prognosis is much worse than in STE-AMI [10]. Finally, the most important thing about this pathology is that multivessel disease is prevalent (up to 80%), and occlusion of the infarct-related artery (IRA) occurs in only 25% of patients [10]. This makes it virtually impossible to clearly identify the target coronary artery to be revascularized. Its identification becomes intuitive, and this can increase the likelihood of inadequate revascularization [11].

Thus, it is highly relevant and clinically significant to determine objective indicators which determine the prognosis of the course of the disease in patients with NSTEMI-AMI after PCI.

Aim

To study the effect of RSS on the mid-term prognosis in patients with NSTEMI-AMI after PCI, and determine the threshold values of RSS for patients with a high and low risk of adverse cardiac events.

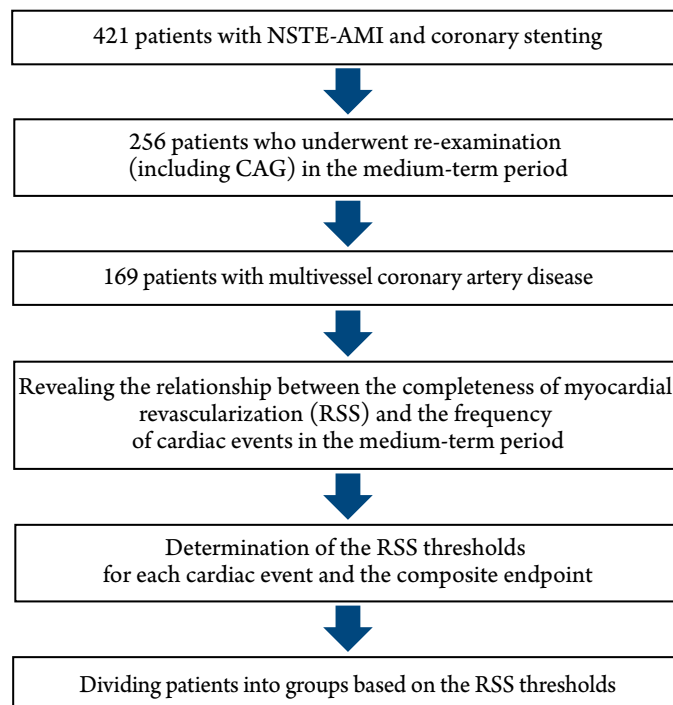
Material and methods

A single-center retrospective study was carried out. The data of 421 patients with NSTEMI-AMI and history of PCI with stenting in the acute period of the disease were analyzed. 169 of these patients with baseline multivessel disease, who were rehospitalized and had coronary angiography (CAG) within the medium-term period (11.7±3.0 months) were selected. The inclusion criteria also included documented elevation in cardiospecific enzymes and the absence of persistent ST-segment elevation. The exclusion criteria were: postinfarction cardiosclerosis; a history of surgical or endovascular myocardial revascularization; severe concomitant pathology; and more than 50% in-stent stenosis according to the repeated CAG after hospital treatment.

The endpoints in the period of interest were: recurrence of clinical manifestations of angina pectoris; repeat revascularization; unstable angina (UA); recurrent AMI; cardiac death; and a composite endpoint of major adverse cardiovascular events (MACE), including UA, recurrent AMI, and cardiac death.

A significant direct relationship between the completeness of revascularization (based on RSS) and the development of unfavorable cardiac events in the follow-up period was revealed at baseline. At this time,

Figure 1. Study design



CAG, coronary angiography.

using ROC analysis, the RSS thresholds were established for each cardiac event and MACE. The patients were divided on that basis into groups of low and high risk of developing the above complications. The study design is shown in Figure 1. The study was performed following the Declaration of Helsinki.

The baseline clinical and anamnestic characteristics of patients are presented in Table 1.

Selective CAG was performed using the Judkins method (1967) and the generally accepted technique. After detailed analysis of the CAG findings and the patient's clinical status, the revascularization strategy was decided. Coronary stenoses ≥70% and stenoses of the left coronary artery ≥50% were considered hemodynamically significant, with the diameter of a vessel ≥1.5 mm [8]. The stenting of two or more coronary arteries (46.2%) was performed mainly in one stage (84.6%), and less often in two stages (15.4%), but during the same period of hospitalization. Bare metal stents were used in 60 (35.5%) patients. The angiographic characteristics of patients are shown in Table 2.

Complete anatomical revascularization (RSS=0) was carried out in 39.1% of cases (n=66). The median RSS was 9 (4; 15) in patients with incomplete correction (n=103, 60.9%).

In hospital, patients received drug therapy in compliance with the 2020 ESC Guideline (Table 3) [10]. During their hospital stay, all patients received

Table 1. Baseline clinical and anamnestic characteristics of patients (n=169)

Parameter	Value
Age, years, M ± SD	61±9.7
Male, n (%)	113 (66.9)
Arterial hypertension, n (%)	146 (86.4)
Smoking, n (%)	68 (40.2)
Diabetes mellitus, n (%)	31 (18.3)
New-onset anginal attack, n (%)	83 (49.1)
Chronic kidney disease, n (%)	13 (7.7)
Creatine kinase MB, mmol/L, Me (Q1; Q3)	50.0 (33.0; 89.0)
Total cholesterol, mmol/L, Me (Q1; Q3)	5.6 (4.7; 6.7)
ECG: ST depression ≥1.5 mm, n (%)	115 (68.0)
ECG: T-wave inversion, n (%)	122 (72.2)
Left ventricular ejection fraction ≤45%, n (%)	21 (12.4)

M ± SD, mean ± standard deviation; Me (Q1; Q3), median and interquartile range (lower quartile; upper quartile).

Table 2. Angiographic characteristics of patient (n=169)

Parameter	Value
BSS score, Me (Q1; Q3)	17 (11; 24)
IRA:	
• LCA trunk, n (%)	7 (4.1)
• LAD, n (%)	78 (46.2)
• LCX, n (%)	43 (25.4)
• RCA, n (%)	41 (24.3)
IRA occlusion, n (%)	37 (21.9)
Chronic coronary occlusion, n (%)	23 (13.6)
Stenting of ≥ 2 coronary arteries, n (%)	78 (46.2)
Number of implanted stents per patient, Me (Q1; Q3)	2 (1; 2)
Patients who had bare metal stents implanted, n (%)	60 (35.5)
Complete revascularization, n (%)	66 (39.1)

BSS, baseline SYNTAX score; IRA, infarction-related artery; LCA, left coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

dual antiplatelet therapy. This was recommended to be continued for up to 6 months, in the case of bare metal stents implanted, and up to 12 months if drug-eluting stents were implanted. At the time of re-examination, patients continued taking acetylsalicylic acid (79.9%), clopidogrel (50.9%), or statins (52.7%).

Statistical processing of the results was carried out using the SPSS Statistics v. 26 suite [12]. The quantitative data is presented as the mean (M) and standard deviation (SD) or the median (Me) and interquartile range (Q1; Q3). The categorical characteristics are expressed as the absolute (n) and relative (%) values. The Student t-test or Mann-Whitney U-tests were used to compare the quantitative indicators, depending on the type of distribution of the variables. The categorical

Table 3. Drug therapy

Parameter	Value
During hospital stay	
Nitrates	45 (26.6%)
Beta-blockers	160 (94.7%)
Angiotensin-converting enzyme inhibitors	142 (84.0%)
Statins	129 (76.3%)
Acetylsalicylic acid	169 (100%)
Clopidogrel	169 (100%)
During the follow-up (11.7±3.0 months)	
Acetylsalicylic acid	135 (79.9%)
Clopidogrel	86 (50.9%)
Statins	89 (52.7%)

Table 4. Comparison of RSS scores depending on the presence and absence of adverse cardiac events in the medium-term period (n=169)

Parameter	RSS, score		P
	in the presence of events Me (Q1; Q3)	in the absence of events Me (Q1; Q3)	
UA, n = 24 (14.2%)	9 (3; 15)	2 (0; 9)	0.004
Recurrent AMI, n = 4 (2.4%)	9.5 (9; 16.5)	3 (0; 10)	0.044
Cardiac death, n = 2 (1.2%)	16.5 (10; 23)	3 (0; 10)	0.079
MACE, n = 28 (16.6%)	9 (3.5; 15)	2 (0; 8)	<0.001
Recurrent manifestations of angina pectoris, n = 79 (46.7%)	3 (0; 10.5)	3 (0; 10)	0.931
Repeat revascularization, n = 94 (55.6%)	4.5 (2; 12)	0 (0; 8)	<0.001

UA, unstable angina; AMI, acute myocardial infarction; MACE, major adverse cardiac events (recurrent AMI, UA, and cardiac death).

indicators were compared using the χ^2 test. ROC analysis was used to determine the threshold values for RSS. The p-value<0.05 was used as the level of statistical significance.

Results

In the medium-term period, 24 (14.2%) patients had UA, 4 (2.4%) patients had recurrent AMI, and 2 patients died of recurrent AMI (Table 4). The frequency of MACE was 16.6% (n=28 patients). Recurrence of the clinical picture of angina pectoris was observed in 79 (46.7%) patients. Repeat revascularization was performed in 94 (55.6%) patients.

A comparison of the RSS indicators in patients with and without adverse cardiac events within the first year showed that this indicator was significantly higher in patients who underwent UA, had recurrent AMI, MACE, and repeat revascularization (see Table 4).

The ROC-curve characterizing the dependence of the risk of developing recurrent AMI on the RSS

Table 5. Angiographic characteristics of patients with $RSS \leq 8$ and $RSS > 8$

Parameter	Group 1, $RSS \leq 8$ (n=117)	Group 2, $RSS > 8$ (n=52)	p
BSS score, Me (Q1; Q3)	13 (10; 19)	26 (19; 33)	<0.001
IRA:			
• LCA trunk, n (%)	5 (4.3)	2 (3.9)	0.773
• LAD, n (%)	63 (53.8)	15 (28.8)	0.003
• LCX, n (%)	26 (22.2)	17 (32.7)	0.150
• RCA, n (%)	23 (19.7)	18 (34.6)	0.037
IRA occlusion, n (%)	20 (17.1)	17 (32.7)	0.024
Chronic coronary occlusion, n (%)	5 (4.3)	18 (34.6)	<0.001
Stenting of ≥ 2 coronary arteries, n (%)	65 (55.6)	13 (25.0)	<0.001
Two-stage stenting, n (%)	10 (8.5)	2 (3.8)	0.440
Number of implanted stents per patient, Me (Q1; Q3)	2 (1; 3)	1 (1; 2)	<0.001
Patients who had bare metal stents implanted, n (%)	42 (35.9)	18 (34.6)	0.873

BSS, baseline SYNTAX score; IRA, infarction-related artery; LCA, left coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

scores is presented in Figure 2 (area under the curve (AUC) 0.79 ± 0.05 ; 95% confidence interval (CI) 0.68–0.89; $p=0.048$). The RSS threshold value at the cut-off point was determined as 8 (sensitivity 100%, specificity 70.9%). Based on this, the patients were divided into Group 2s, in order to predict recurrent AMI: Group 1 with $RSS \leq 8$; and Group 2 with $RSS > 8$. In Group 1, there were no cases of recurrent AMI, while 4 (2.4%) patients in Group 2 developed this complication.

The baseline clinical and anamnestic characteristics are presented in Table 1, and they were mostly comparable between the groups ($p > 0.05$). However, the mean age of patients in Group 2 (64 ± 11.8 years)

was significantly higher than in Group 1 (60 ± 8.4 years; $p=0.026$). All patients had ST-segment depression ($n=169$), but more than 1.5 mm depression was more common in Group 2 (78.8% vs. 63.2%, respectively; $p=0.045$).

According to CAG (Table 5), both IRA occlusion (32.7% vs. 17.1%, respectively; $p=0.024$) and chronic coronary artery occlusion (34.6% vs. 4.3%, respectively; $p < 0.001$) were observed much more often in Group 2. Left anterior descending artery was considered an IRA significantly more often in Group 1 (53.8% vs. 28.8%, respectively; $p=0.003$), while RCA prevailed in Group 2 (34.6% vs. 19.7%, respectively; $p=0.037$). There was no statistically significant

Figure 2. ROC-curve characterizing the dependence of the risk of recurrent myocardial infarction on the RSS score

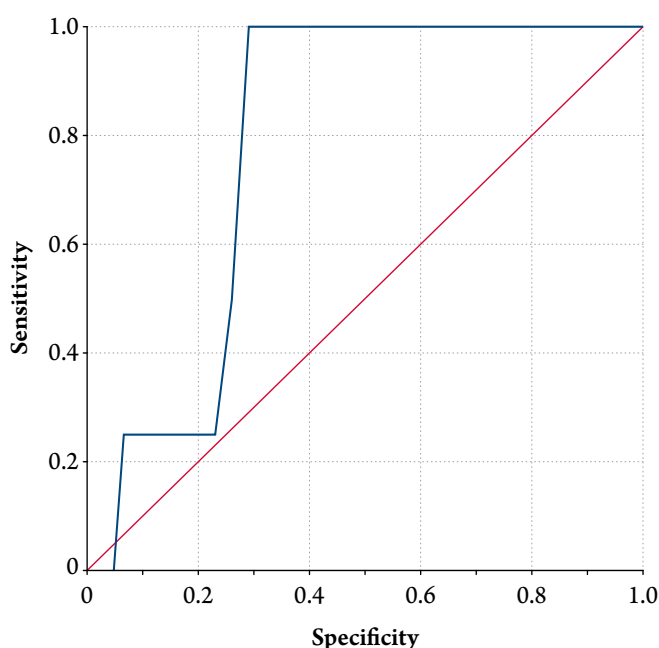


Figure 3. ROC-curve characterizing the dependence of the risk of unstable angina on the RSS score

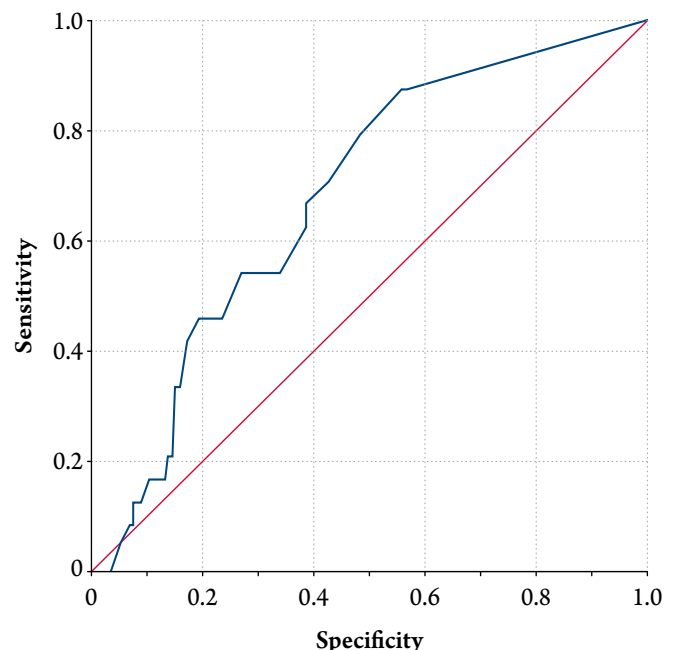


Table 6. Angiographic characteristics of patients with RSS <3 and RSS ≥3

Parameter	Group 1, RSS <3 (n=80)	Group 2, RSS ≥3 (n=89)	P
BSS score, Me (Q1; Q3)	12 (10; 18)	20 (14; 30)	<0.001
IRA:			
• LCA trunk, n (%)	3 (3.7)	4 (4.5)	0.886
• LAD, n (%)	43 (53.8)	35 (39.3)	0.061
• LCX, n (%)	19 (23.7)	24 (27.0)	0.632
• RCA, n (%)	15 (18.8)	26 (29.2)	0.114
IRA occlusion, n (%)	12 (15.0)	25 (28.1)	0.040
Chronic coronary occlusion, n (%)	2 (2.5)	21 (23.6)	<0.001
Stenting of ≥2 coronary arteries, n (%)	60 (75.0)	18 (20.2)	<0.001
Two-stage stenting, n (%)	9 (11.3)	3 (3.4)	0.091
Number of implanted stents per patient, Me (Q1; Q3)	2 (2; 3)	1 (1; 2)	<0.001
Patients who had bare metal stents implanted, n (%)	26 (32.5)	34 (38.2)	0.440

BSS, baseline SYNTAX score; IRA, infarction-related artery; LCA, left coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

difference in the type of coronary circulation. The stenting of two or more coronary arteries was performed significantly more often in Group 1 (55.6% vs. 25.0%, respectively; $p<0.001$). Group 1 had a higher number of implanted stents per patient (median 2 vs. 1; $p<0.001$). The percentage of two-stage stenting did not differ significantly between the groups (8.5% vs. 3.8%, respectively; $p=0.440$), nor did the number of patients who had bare metal stents implanted (35.9% vs. 34.6%, respectively; $p=0.873$).

There were significant differences between Group 1 and Group 2 in the frequency of drug use during the hospital stay ($p>0.05$). At the time of the second examination (11.7±3.0 months), the percentage of patients who continued taking acetylsalicylic acid, clopidogrel, and statins were also comparable in the groups ($p>0.05$).

The ROC-curve characterizing the dependence of the risk of developing HC on the RSS scores is presented in Figure 3 (AUC=0.68±0.05; 95% CI: 0.58–0.79; $p=0.005$). The RSS threshold was 3 at the cut-off point. On that basis, the patients were divided into Group 2s, in order to predict UA: Group 1 with RSS<3; and Group 2 with RSS>3. Results showed that the chances of developing UA were 4.07 times higher in Group 1 than in Group 2 (95% CI: 1.44–11.49; $p=0.01$). The sensitivity and specificity were 79.2% and 51.7%, respectively. The low specificity should not be alarming in this case, since all patients with false-positive results have baseline incomplete revascularization with RSS ≥3. Re-examination with possible endovascular treatment is indicated for them.

The groups were mainly comparable in terms of the baseline clinical and anamnestic data ($p>0.05$). However,

the ST-segment depression>1.5 mm was significantly more frequent in patients with RSS ≥3 (77.5% vs. 57.5%, respectively; $p=0.006$).

According to CAG (Table 6), both IRA occlusions (28.1% vs. 15.0%, respectively; $p=0.040$) and chronic coronary artery occlusions (23.6% vs. 2.5%, respectively; $p<0.001$) were observed significantly more often in Group 2. There were no significant differences in the localization of IRA ($p>0.05$). The stenting of two or more coronary arteries was significantly more common in Group 1 (75.0% vs. 20.2%, respectively; $p<0.001$), as was the number of implanted stents per patient (median 2 vs. 1; $p<0.001$). The frequency of two-stage stenting did not differ significantly between the groups (11.3% vs. 3.4%, respectively; $p=0.091$). There was no significant intergroup difference in the number of patients with bare-metal stents implanted (32.5% in Group 1 vs. 38.2% in Group 2; $p=0.440$).

The groups did not differ significantly in terms of the drug therapy during the hospital stay. At the second examination, the percentage of patients continuing to take acetylsalicylic acid, clopidogrel, and statins were also comparable in the groups ($p>0.05$).

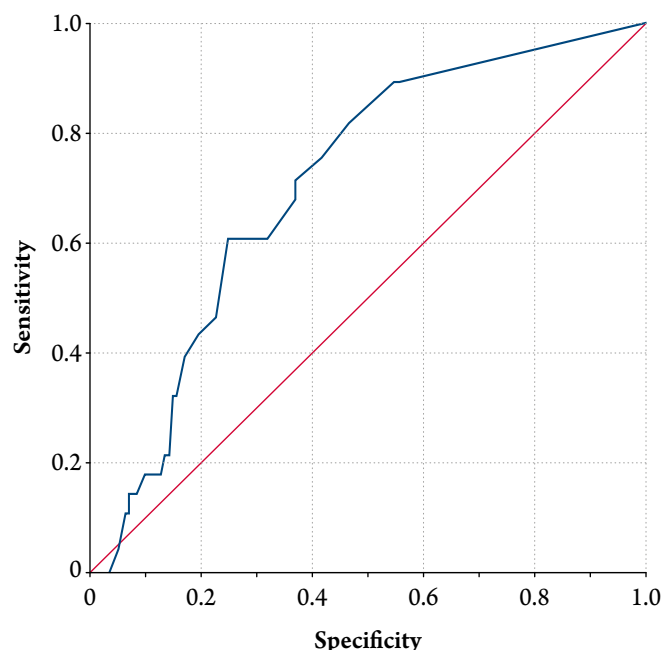
The ROC-curve characterizing the dependence of the risk of developing MACE on the RSS scores is presented in Figure 4 (AUC=0.71±0.05; 95% CI: 0.61–0.8; $p=0.001$). The RSS threshold value at the cut-off point was determined, as for UA, equal to 3 (sensitivity 82.1%, specificity 53.2%). The likelihood of developing MACE with RSS≥3 was 5 times as high as with RSS<3 (odds ratio 5.23, 95% CI: 1.88–14.53; $p=0.001$). UA was the most common MACE (85.7%), while recurrent AMI and cardiac death accounted for 14.3%.

Индапамид + периндоприл



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Figure 4. ROC-curve characterizing the dependence of the risk of MACE on the RSS score



Therefore the RSS threshold values for UA and MACE were the same.

Discussion

Due to their high clinical, anamnestic, anatomical, and angiographic heterogeneity, patients with NSTEMI-AMI present more significant difficulties in the choice of treatment strategies [1, 10]. Therefore, the maximum objectification of the prognosis of possible complications after hospital treatment is especially important for this category of patients, in order to prevent them [13, 14]. To determine the risk of adverse cardiac events after PCI [2–7], we chose the SYNTAX angiographic score as an instrument.

Our study of the effects of the completeness of myocardial revascularization on the medium-term prognosis in patients with NSTEMI-AMI confirmed the opinion of many authors that RSS values were significantly higher in patients with cardiac complications when compared with patients without cardiac complications [2, 3, 5–7, 14, 15]. At the same time, ROC analysis ($AUC=0.79\pm0.05$; 95% CI 0.68–0.89; $p=0.048$) enabled us to establish the RSS threshold for the risk of developing recurrent AMI equal to 8 (sensitivity 100%, specificity 70.9%). Patients with $RSS \leq 8$ did not have a single case of recurrent AMI.

This complication was observed in 2.4% ($n=4$) of cases with $RSS>8$. This result is consistent with a number of Russian and foreign researchers [2, 3, 14].

The threshold value of RSS was 3 for UA and MACE. At the same time, the probability of UA within one year was 4.07 times, and MACE was 5.23 times higher with $RSS \geq 3$ than with lower RSS scores (95% CI: 1.44–11.49; $p=0.01$ and 95% CI: 1.88–14.53; $p=0.001$, respectively). It should be noted that the groups identified in terms of RSS were comparable in terms of clinical and anamnestic characteristics.

Therefore, in accordance with contemporary literature, the completeness of revascularization largely determines the outcome of patients with ACS. This was also confirmed in our study, such as in patients with NSTEMI-AMI. However, there is still no unambiguous opinion about the target value of RSS, if complete revascularization is impossible in various forms of ACS. We established threshold values for RSS which determine the high risk of recurrent AMI (>8), UA, and MACE (≥ 3) in patients with NSTEMI-AMI in the medium-term period. These indicators can presumably be used to optimize recommendations for the PCI strategy, as well as the management of patients with NSTEMI-AMI after hospital treatment.

Limitations

This study was limited by its retrospective, non-randomized, and non-multicenter design and relatively small patient sample size. However, our work is based on the analysis of data from the most homogeneous patient sample using modern research and data processing methods, enabling us to obtain some reliable results.

Conclusion

The study demonstrated the high predictive significance of the SYNTAX Score (RSS) of residual coronary artery disease in patients with non-ST-segment elevation acute myocardial infarction during the first year of follow-up. The quantitative data obtained in the form of RSS thresholds can be helpful in choosing the volume of revascularization and for scheduling timely re-examination and treatment, in order to prevent cardiovascular complications after hospital treatment.

No conflict of interest is reported.

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