

Article

Discrepancy between the European clinical guidelines and myocardial revascularization in patients with stable coronary artery disease in Russia

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Abstract

Objective: In European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines, six indications have been proposed for making a decision on myocardial revascularization in patients with stable coronary artery disease (CAD). Our aim was to study a discrepancy between the actual clinical situation and ESC/EACTS indications on performing the revascularization in patients with CAD in Russia.

Design and setting: We used retrospective clinical data on patients with stable CAD enrolled in the 2012–2015 Russian Registry of Hypertension, Coronary Artery Disease, and Chronic Heart Failure.

Participants: A total of 1522 patients with CAD (aged 53.0 ± 8.5 years, 76.2% male) were used for analysis.

Interventions: All patients were divided into two groups: 591 patients with performed myocardial revascularization (named as R-CAD) and 931 patients refused from revascularization (named as NR-CAD). Factors associated with revascularization performance were identified by discriminant function analysis.

Main outcome measures: ESC/EACTS indications for revascularization were assessed.

Results: A total of 1196 patients with CAD had any ESC/EACTS indication for revascularization, but only 40.2% of them had performed invasive coronary intervention. Myocardial revascularization was appropriate in 81.4% of R-CAD patients and 76.8% of NR-CAD patients. The main factor of revascularization performance was any stenosis $>50\%$ and grades III–IV of stable angina. With non-performed revascularization, the following factors were associated: limiting angina or angina equivalent, unresponsive to medical therapy, atherosclerotic peripheral arterial disease and increasing the New York Heart Association class of chronic heart failure. Most ESC/EACTS indications had little effect on decision-making on revascularization.

Conclusion: There is a discrepancy between the actual clinical situation and ESC/EACTS guidelines on myocardial revascularization in patients with stable CAD in Russia.

Key words: coronary artery disease, myocardial revascularization, ESC/EACTS guidelines, clinical indications

Introduction

Coronary artery disease (CAD) is still the main cause of death in the world [1, 2] and Russia in particular [3]. Quality and effectiveness of health care in patients with CAD is still the actual problem of Russian cardiology [4, 5].

The importance of the problem of myocardial revascularization in patients with stable CAD is obvious. Many authors have studied the efficiency of this intervention, including the decision-making [6], appropriateness [7], quality of life [8], outcomes [9–11], etc. Performing the coronary artery bypass grafting and percutaneous coronary intervention reduces the severity of myocardial ischemia and the need of emergency operations for myocardial revascularization in future in patients with stable CAD [12]. At the present time, there is no evidence yet of the effectiveness of percutaneous coronary intervention in the prevention of death, non-fatal myocardial infarction and hospitalization with acute coronary syndrome [13, 14]. The studies of this problem are still going on. For example, the positive preventive effect of coronary artery bypass grafting in patients with stable CAD, in particular with stenosis of the left coronary artery and multivessel lesions, has been convincingly proved [15, 16].

In clinical guidelines of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) (2014), it is indicated that the aim of coronary intervention is to reduce symptoms and improve prognosis. This aim is consistent with the general principles of CAD treatment [17]. According to these guidelines, six indications must be used for decision-making on myocardial revascularization in patients with stable form of CAD (the full list of indicators is presented in Material and Methods section). These indications are designed to increase the appropriateness and prompt implementation of revascularization in patients, who need intervention, and also to avoid them in patients, whose treatment may be limited to drug therapy.

Not much is known about quality and national features of invasive strategy of CAD treatment in Russia. The primary objective of this study is to determine a discrepancy between the actual clinical situation and ESC/EACTS guidelines on performing the myocardial revascularization in patients with stable CAD in Russia.

Material and Methods

Data source

The Russian Registry of Hypertension, Coronary Artery Disease and Chronic Heart Failure (RusR-Htn-CAD-CHF) [18] was used as a source of data about patients with stable CAD in Russia. The RusR-Htn-CAD-CHF is a retrospective, continuous, nationwide, web-based registry operating online. Participation in this registry is voluntary. The access to the registry is given only to registered members. The source of patients' data is a patient medical card and/or hospital chart. Each patient has fulfilled an informed consent form prior to his/her data to be included in the database of the RusR-Htn-CAD-CHF. Details of design of the RusR-Htn-CAD-CHF are presented in our previous publications [18, 19].

Patient selection

We used the following criteria to enroll the patients in this study:

- (i) diagnosis of stable angina, old myocardial infarction and other forms of chronic ischemic heart disease in accordance with the International Classification of Diseases 10 version,
- (ii) age ≥ 18 years,
- (iii) coronary angiography result for 2012–5,
- (iv) echocardiography with determination of left ventricular ejection fraction (LVEF), conducted not earlier than 12 months before the myocardial revascularization in patients with performed revascularization or not earlier than 12 months before and not later than 12 months after the date of coronary angiography in patients refused from revascularization.

The patients were not included in our study, if they had acute coronary syndrome during the previous 30 days.

Patients

Retrospective clinical data on 1522 patients with stable CAD (aged 53.0 ± 8.5 years, 76.2% male) enrolled in the 2012–2015 RusR-Htn-CAD-CHF and meeting the inclusion/exclusion criteria were examined. Patients were selected randomly from the database of the RusR-Htn-CAD-CHF.

After inclusion into study, all patients were divided into two groups according to the presence or absence of myocardial revascularization in 2012–5. The first group was composed of 591 patients (38.8%) with performed revascularization. This group was named as 'R-CAD patients.' The second group was composed of 931 patients (61.2%) refused from revascularization. This group was named as 'NR-CAD patients.'

Indications for myocardial revascularization

We used the following ESC/EACTS indications [17] for myocardial revascularization in patients with stable CAD:

- (i) left main disease with stenosis $>50\%$ (class of recommendation and level of evidence: IA),
- (ii) any proximal stenosis of left anterior descending coronary artery (LAD) $>50\%$ (class of recommendation and level of evidence: IA),
- (iii) two- or three-vessel disease with stenosis $>50\%$ with LVEF less than 40% (class of recommendation and level of evidence: IA),
- (iv) large area of ischemia (over 10% of the left ventricle) (class of recommendation and level of evidence: IB),
- (v) single remaining patent coronary artery with stenosis $>50\%$ (class of recommendation and level of evidence: IC),
- (vi) any coronary stenosis $>50\%$ in the presence of limiting angina or angina equivalent, unresponsive to medical therapy (class of recommendation and level of evidence: IA). Here, medical therapy is understood as a treatment including drugs for cardiovascular prevention and at least one anti-angina drug.

Appropriateness of myocardial revascularization was determined, if at least one of these ESC/EACTS indications was present. Note that in the ESC/EACTS guidelines there is no clear definition of the term 'limiting angina.' In this study, stable angina grade II and above was interpreted as limiting angina, which can limit the daily activity of

patients with CAD, which is consistent with the opinion of Frattaroli *et al.* [20].

Design of analysis

This study was approved by the local Ethics Committee of Saratov State Medical University n.a. V.I. Razumovsky (Saratov, Russia). First, we performed the comparison of R-CAD and NR-CAD patients by all clinical characteristics. We have identified clinical features for both patients' groups.

Then, we assessed the prevalence of ESC/EACTS indications for myocardial revascularization in R-CAD and NR-CAD patients. Next, clinical parameters, which differed in R-CAD and NR-CAD patients at $P < 0.1$, and ESC/EACTS indications were included to multiple logistic regression analysis for identifying the main factors associated with myocardial revascularization performance.

Statistical analysis

We applied the Shapiro–Wilk test to check whether the data were approximately normally distributed. We applied the Chi-square (χ^2) test to compare the binary variables and to compute the significance level for the difference between two proportions. Mann–Whitney test was used to compare the continuous non-normal distributed variables; t -test was used for normal distributed continuous variables. Categorical variables, including binary (Yes/No), are presented as frequencies and percentages. Continuous variables are reported as medians (Me) and interquartile ranges (LQ, UQ) for non-normal distribution, and as mean (M) with standard deviation (SD) for normal distribution.

We used multiple logistic regression to evaluate the clinical characteristics and ESC/EACTS indications as potential factors associated with myocardial revascularization performance. As a preliminary step to the logistic analysis, a receiver operating characteristic (ROC) analysis and Youden index were used to identify effective cut-off points for each of the continuous variables in order to distinguish the patients in accordance with the implementation of revascularization. We did not include perfect collinear variables in the analysis. In other cases of collinearity, we did not change the list of variables included into the multiple analysis.

The obtained estimations were considered statistically significant, if $P < 0.05$.

Results

Characteristics of R-CAD and NR-CAD patients

Clinical characteristics of R-CAD and NR-CAD patients enrolled in this study are presented in Table 1. It was found that R-CAD and NR-CAD patients differ in most clinical characteristics. R-CAD patients had the following peculiarities in comparison with NR-CAD patients (Table 1):

- (i) the proportion of men was slightly higher,
- (ii) they were slightly older than NR-CAD patients,
- (iii) they were more likely to have old myocardial infarction and atherosclerotic peripheral arterial disease,
- (iv) they had stable angina of lesser severity (including complaints of chest pain and typical angina pectoris) and comorbidities (hypertension, chronic heart failure and diabetes),
- (v) they had somewhat less the levels of blood pressure, heart rate, total cholesterol, triglycerides and high-density lipoprotein,

- (vi) they had somewhat higher values of glomerular filtration rate and the prevalence of coronary stenosis $>70\%$. Note that 12 R-CAD patients had no significant stenosis.

Prevalence of ESC/EACTS indications for myocardial revascularization in R-CAD and NR-CAD patients

In the studied groups of patients, we identified two factors limiting the individual testing of some ESC/EACTS indications for myocardial revascularization: the absence of patients with the results of stress echocardiography and the absence of patients with a single remaining patent coronary artery. Therefore, further we used only the following ESC/EACTS indications:

- (i) left main disease with stenosis $>50\%$,
- (ii) any proximal stenosis of LAD $>50\%$,
- (iii) two- or three-vessel disease with stenosis $>50\%$ with LVEF $<40\%$,
- (iv) any coronary stenosis $>50\%$ in the presence of limiting angina or angina equivalent, unresponsive to medical therapy.

Prevalence of these indications in the studied groups of patients is presented in Table 2. We did not identify any statistically significant difference between the groups. Given the possible individual combination of ESC/EACTS indicators, the performed myocardial revascularization was appropriate only in 81.4% of R-CAD patients (481/591), whereas 76.8% of NR-CAD patients (715/931) needed invasive treatment. The prevalence of various combinations of ESC/EACTS indications for myocardial revascularization in R-CAD and NR-CAD patients is presented in Table 3.

Thus in our study, 1196 patients with CAD (78.6% of total group) had any ESC/EACTS indication for myocardial revascularization, but only 40.2% of them (481 patients) had performed the invasive coronary intervention.

Association between the patients' clinical characteristics, ESC/EACTS indications and myocardial revascularization performance

We attempted to identify the cut-off points for each of the continuous variables in Table 1 (age, blood pressure, heart rate, body mass index, glomerular filtration rate, LVEF, blood glucose, total cholesterol, triglycerides, low- and high-density lipoproteins, creatinine and hemoglobin) in order to distinguish between the subjects in accordance with the implementation of revascularization (R-CAD or NR-CAD patients) based on ROC analysis. However, the area under the ROC curve (AUC) was less than 0.6 for all studied continuous variables. This fact allowed us to consider these continuous variables as bad classifiers for R-CAD or NR-CAD patients. There was no expediency in determining the cut-off points. Thus, these continuous variables were not included in the logistic regression analysis.

All binary clinical characteristics (see Table 1) and ESC/EACTS indications were included in the logistic regression analysis for the distinction between R-CAD and NR-CAD patients. The results of logistic regression analysis are presented in Table 4. Overall Model Fit: Chi-square = 656.3, $df = 22$, $P < 0.001$. Percent of cases correctly classified in R-CAD and NR-CAD patients was 76.5 and 83.2%, respectively (AUC was 0.856, 95% CI: 0.838–0.874). Therefore, the main clinical factors associated with myocardial revascularization performance in the studied patients with stable CAD were stable angina (Grades III–IV) and any stenosis $>50\%$ in

Table 1 Baseline characteristics of patients with CAD included in the study

Parameters	R-CAD patients (n = 591)	NR-CAD patients (n = 931)	P level
Demographic and clinical characteristics			
Male sex, % (n/N)	81.4 (481/591)	72.8 (678/931)	<0.001
Age, years, M ± SD	53.9 ± 8.9	52.4 ± 8.2	<0.001
Old myocardial infarction, % (n/N)	67.9 (401/591)	57.0 (531/931)	<0.001
Stable angina, % (n/N)	82.6 (488/591)	94.8 (883/931)	<0.001
Grade of stable angina, % (n/N)			
I	11.5 (56/488)	8.0 (71/883)	0.032
II	51.8 (253/488)	59.4 (524/883)	0.007
III	35.9 (175/488)	32.5 (287/883)	0.203
IV	0.8 (4/488)	0.1 (1/883)	0.036
Complaints of chest pain, % (n/N)	77.1 (437/591)	94.5 (883/931)	<0.001
Typical angina pectoris, % (n/N)	55.1 (306/555)	64.8 (596/920)	<0.001
Hypertension, % (n/N)	90.2 (533/591)	93.8 (873/931)	0.009
CHF, % (n/N)	87.3 (516/591)	95.5 (889/931)	<0.001
NYHA CHF class, % (n/N)			
I	37.2 (192/516)	16.8 (149/889)	<0.001
II	48.1 (248/516)	66.3 (589/889)	<0.001
III	14.3 (74/516)	16.5 (147/889)	0.275
IV	0.4 (2/516)	0.4 (4/889)	1.000
Prior stroke, % (n/N)	5.6 (33/591)	3.9 (36/931)	0.122
APAD, % (n/N)	11.2 (66/591)	15.9 (148/931)	0.010
Diabetes mellitus, % (n/N)	14.6 (56/591)	18.5 (172/931)	0.049
Smoking, % (n/N)	29.5 (135/457)	32.8 (243/740)	0.233
SBP at last visit, mmHg, M ± SD	132.3 ± 20.0	134.7 ± 18.6	0.003
DBP at last visit, mmHg, M ± SD	81.3 ± 10.4	83.4 ± 9.8	<0.001
HR at last visit, beats/min, M ± SD	68.1 ± 8.1	69.3 ± 9.3	0.016
BMI, kg/m ² , Me (LQ, UQ)	28.7 (26.0, 32.3)	28.7 (25.7, 31.8)	0.309
LVEF, %, Me (LQ, UQ)	61.0 (54.0, 66.0)	61.0 (53.0, 65.0)	0.844
Blood glucose, mmol/l, Me (LQ, UQ)	5.4 (4.8, 6.1)	5.2 (4.7, 6.1)	0.066
Total cholesterol, mg/dl, Me (LQ, UQ)	174.4 (145.5, 210.5)	186.0 (151.2, 217.1)	0.008
Triglycerides, mg/dl, Me (LQ, UQ)	116.9 (83.3, 166.7)	126.3 (92.1, 166.7)	0.063
LDL, mg/dl, Me (LQ, UQ)	114.0 (90.0, 130.0)	116.3 (87.6, 134.5)	0.779
HDL, mg/dl, Me (LQ, UQ)	45.0 (38.8, 50.0)	46.2 (40.0, 52.8)	0.003
Creatinine, mg/dl, Me (LQ, UQ)	88.0 (77.0, 96.8)	88.0 (70.4, 96.8)	0.331
GFR, ml/min, Me (LQ, UQ)	102.9 (88.2, 120.8)	97.7 (82.0, 115.9)	<0.001
Hemoglobin, g/l, Me (LQ, UQ)	145.0 (134.0, 153.0)	143.0 (134.0, 152.0)	0.524
Coronarography results			
Any stenosis >70%, % (n/N)	95.1 (562/591)	76.0 (708/931)	<0.001
Any stenosis 50–69%, % (n/N)	2.9 (17/591)	7.0 (65/931)	<0.001
Any stenosis <50% or absence, % (n/N)	2.0 (12/591)	17.0 (158/931)	<0.001

M ± SD is mean with standard deviation. Me (LQ, UQ) are median and interquartile ranges. (n/N) is the number of patients with the presence of parameter and total number of patients with data on this parameter.

APAD, atherosclerotic peripheral arterial disease; BMI, body mass index; CHF, chronic heart failure; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL, high-density lipoprotein; HR, heart rate; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; NYHA, the New York Heart Association; SBP, systolic blood pressure.

Table 2 Prevalence of ESC/EACTS indications for myocardial revascularization in R-CAD and NR-CAD patients

Parameters	R-CAD patients (n = 591)	NR-CAD patients (n = 931)	P level
Left main disease with stenosis >50%, % (n/N)	4.9 (29/591)	7.2 (67/931)	0.072
Any proximal stenosis of LAD >50%, M ± SD	36.2 (214/591)	31.8 (296/931)	0.077
Two- or three-vessel disease with stenosis >50% with LVEF <40%, % (n/N)	3.9 (23/591)	2.4 (22/931)	0.094
Any coronary stenosis >50% in the presence of limiting angina or angina equivalent, unresponsive to medical therapy, % (n/N)	71.7 (424/591)	72.4 (674/931)	0.766

(n/N) is the number of patients with the presence of parameter and total number of patients with data on this parameter. LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction.

Table 3 Prevalence of combinations of ESC/EACTS indications for myocardial revascularization in R-CAD and NR-CAD patients

No.	Left main disease with stenosis >50%	Any proximal stenosis of LAD >50%	Two- or three-vessel disease with stenosis >50% with LVEF <40%	Any coronary stenosis >50% in the presence of limiting angina or angina equivalent, unresponsive to medical therapy	R-CAD patients (n = 591)	NR-CAD patients (n = 931)	P level
1	✓				0.7 (4/591)	0.2 (2/931)	0.129
2		✓			8.6 (51/591)	3.5 (33/931)	<0.001
3			✓		0.2 (1/591)	0.4 (4/931)	0.502
4				✓	39.6 (234/591)	40.0 (372/931)	0.877
5	✓	✓			0.2 (1/591)	0.1 (1/931)	0.670
6	✓		✓		0	0.1 (1/931)	0.442
7	✓			✓	2.5 (15/591)	3.7 (34/931)	0.197
8		✓	✓		0	0	1.000
9		✓		✓	24.7 (146/591)	24.1 (224/931)	0.790
10			✓	✓	2.0 (12/591)	0.4 (4/931)	0.003
11	✓	✓	✓		0	0	1.000
12	✓	✓		✓	1.2 (7/591)	2.9 (27/931)	0.029
13	✓		✓	✓	0.2 (1/591)	0.2 (2/931)	1.000
14		✓	✓	✓	1.4 (8/591)	1.2 (11/931)	0.735
15	✓	✓	✓	✓	0.2 (1/591)	0	0.172

Data presented as % (n/N). (n/N) is the number of patients with the presence of parameter and total number of patients with data on this parameter. LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction.

Table 4 Results of the logistic regression analysis

Variables	OR (95% CI)
Any coronary stenosis >50% in the presence of limiting angina or angina equivalent, unresponsive to medical therapy	0.07 (0.06–0.09)
CHF: NYHA class II	0.28 (0.17–0.46)
CHF: NYHA class III	0.32 (0.18–0.59)
CHF: NYHA class IV	0.45 (0.06–3.40)
APAD	0.46 (0.30–0.69)
Left main disease with stenosis >50%	0.58 (0.33–1.03)
CHF: NYHA class I	0.62 (0.36–1.06)
Smoking	0.75 (0.54–1.03)
Typical angina pectoris	0.86 (0.62–1.19)
Diabetes mellitus	0.90 (0.62–1.29)
Hypertension	0.98 (0.60–1.60)
Any proximal stenosis of LAD >50%	0.99 (0.74–1.32)
Old myocardial infarction	1.11 (0.83–1.47)
Male sex	1.35 (0.97–1.89)
Prior stroke	1.45 (0.72–2.92)
Two- or three-vessel disease with stenosis >50% with LVEF <40%	1.49 (0.71–3.13)
Stable angina: Grade II	1.65 (0.99–2.72)
Stable angina: Grade I	1.86 (0.91–3.54)
Stable angina: Grade III	2.78 (1.60–4.81)
Any stenosis 50–69% in CG result	18.88 (7.67–46.48)
Stable angina: Grade IV	24.16 (1.76–332.44)
Any stenosis >70% in CG result	39.38 (20.40–76.03)

Data presented as odds ratio with 95% confidence intervals – OR (95% CI).

APAD, atherosclerotic peripheral arterial disease; CG, coronarography; CHF, chronic heart failure; LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction; NYHA, the New York Heart Association.

coronarographic result (see Table 4). Such factors as any coronary stenosis >50% in the presence of limiting angina or angina equivalent, unresponsive to medical therapy, chronic heart failure (NYHA

classes II–III) and atherosclerotic peripheral arterial disease (see Table 4) were associated with the refuse from revascularization in the studied patients.

Discussion

Our findings indicated that the prevalence of the left main disease with stenosis >50% was 6.3% in the studied patients with stable CAD in Russia. Frequency of occurrence of this stenosis from data of international literature varies from 3% to 5% [21]. In the Tyumen Cardiology Center, Kuznetsov *et al.* reported on the results similar to our results: left main disease was detected in 6% of CAD patients [22]. According to Litvinenko *et al.*, prognostically unfavorable lesion of the proximal segment of anterior descending artery occurred in 42.9% of patients, which also indicates the severity of coronary atherosclerotic lesion in CAD patients in Russia [23].

We have shown that patients with conservative treatment (NR-CAD group) usually had a more severe clinical status, including comorbidities and prevalence of typical angina pectoris, whereas R-CAD patients often had an old myocardial infarction. Attention is drawn to the fact that in R-CAD patients before myocardial revascularization, the angina was less common and with its presence the characteristics of chest pain were less typical (see Table 1: complaints of chest pain vs typical angina pectoris). The results of multiple logistic regression analysis have shown that the presence of ESC/EACTS indications for myocardial revascularization in CAD patient does not determine the tactics of patient management. The decision to perform the myocardial revascularization was determined, if any coronary stenosis was >50%. This case was often accompanied by low-grade angina pectoris. In contrast, limiting angina or angina equivalent, unresponsive to medical therapy in a patient with chronic heart failure served as a reason for choosing a conservative treatment strategy. As a result, 18.6% of R-CAD patients had no ESC/EACTS indications for myocardial revascularization and for 76.8% of NR-CAD patients, an invasive treatment can be advisable. These indices could be significantly higher in

determining the limiting angina pectoris, as stable angina grade III and above [24].

The considered multiple logistic regression model based on different clinical factors is able to describe 83.2% of NR-CAD patients. In our opinion, this result confirms the impact of severe clinical status (chronic heart failure, limiting angina and atherosclerotic peripheral arterial disease) on refusing the myocardial revascularization. For example, the refuse of myocardial revascularization in patients with left main disease may be associated with different clinical reasons (contraindications, high intraoperative risks, and lack of technical capability), as well as the refusal of patients from surgery [22].

The considered above problems require a solution. To avoid this situation, the American College of Cardiology Foundation (ACCF) and some other organizations have developed the appropriate use criteria for coronary revascularization, which take into account the potential benefit and risks for patient [25, 26]. In our previous article in Russian [27], we reported on the perspectives of using similar criteria in patients with stable CAD in Russia. The Russian Society of Cardiology traditionally proposes to use clinical guidelines of the ESC in clinical practice. Therefore, it is important to develop such appropriate use criteria on the basis of existing ESC guidelines. Practical implementation of these criteria can be carried out on the basis of the RusR-Htn-CAD-CHF.

The strength of our study is the analysis of combinations of several factors in addition to the analysis of single factors associated with indications for myocardial revascularization. It allows us to examine in detail the reasons for performance and refuse from performance of revascularization in different clinical situations.

Conclusion

There is a discrepancy between the actual clinical situation and existing ESC/EACTS guidelines in terms of myocardial revascularization performance in patients with stable CAD in Russia. Most patients (59.8%) included in our study and having indications for myocardial revascularization have not undergone an invasive treatment strategy. At the same time, 18.6% of revascularization was performed not according to the ESC/EACTS indications.

Limitations

A limitation of our study is its retrospective character. It would be better to carry out a prospective study for estimating the influence of different clinical factors on making a decision on myocardial revascularization. However, such task is much more difficult than the analysis of data from the RusR-Htn-CAD-CHF.

Frequency of occurrence of some combinations of indications for myocardial revascularization is rather small and such combinations take place only in several subjects (see Table 3). As the result, the influence of these rare combinations on the results of our study is small. In future, we plan to carry out a similar study, which will include another period of time and greater number of patients.

Since we did not have detailed data on contraindications to revascularization, we were not able to take into account their direct influence on the refuse from the revascularization performance. We assume that this fact reduced the coverage of the considered multiple logistic regression model for NR-CAD patients.

Our study included the period of time from 2012 to 2015. However, for some NR-CAD patients included in the study, the revascularization was performed in 2016. This revascularization

was not taken into account. Since the part of coronary intervention performed in December 2015 was 1.3%, the possible error of our results is small.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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