Features and hospital outcomes of coronary artery bypass grafting in patients with calcification of target coronary arteries

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Aim. To compare strategy and early results of coronary artery bypass grafting (CABG) in patients with and without calcification of target coronary arteries (TCA).

Material and methods. The prospective study analyzed the data of patients (n=462) who underwent elective isolated CABG in 2017-2018 using cardiopulmonary bypass and microsurgery. Two groups were distinguished: group 1 — patients with TCA calcification (n=108), group 2 — patients without TCA calcification (n=354). In cases where the distal coronary artery lesion did not allow standard bypass grafting, additional complex anastomoses were provided. A comparison of intraoperative parameters and early results of CABG was carried out.

Results. In groups 1 and 2, the revascularization index did not differ significantly and was 4,5 and 4,3, respectively. The frequency of complex surgical interventions in group 1 was higher: for example, 'Y' grafts were used in groups 1 and 2, respectively, in 32% (35/108) and 12% (44/354), p<0,05; sequential anastomoses — in 14% (15/108) and 7% (26/354), p<0,05; prolonged patch-angioplasty — in 21% (23/108) and 5% (16/354), p<0,05; anastomoses with arteries <1,5 mm in diameter — in 33% (36/108) and 4% (14/354), p<0,05; coronary endarterectomy — in 17% (18/108) and 5% (16/354), p <0.05, respectively. The duration of cardio-pulmonary bypass was longer in group 1. At the same time, the hospital clinical results did not differ significantly: mortality was not registered; the frequency of perioperative myocardial infarction was 1,8% (group 1) and 1,1% (group 2); the need for inotropes, frequency of arrhythmia, length of stay in the intensive care unit and hospital were similar; there were no cases of in-hospital angina recurrence.

Conclusion. CABG in patients with calcification of TCA is associated with surgical challenges and need for complex adjunct techniques. Nevertheless, complete surgical revascularization is real in these cases, and the hospital results are comparable to those in patients without calcification.

Key words: coronary artery calcinosis, coronary artery disease, coronary artery bypass grafting.

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The widespread introduction of endovascular surgery and modern drug treatment of coronary artery disease (CAD) into clinical practice has led to the fact that in recent years, surgeons increasingly operate on elderly patients with severe coronary artery (CA) lesion, history of stenting (including repeated) and many comorbidities. Hypertension, obesity, dyslipidemia, hyperglycemia, familial predisposition, chronic kidney disease, high levels of fibrinogen and C-reactive protein increases the risk of CA calcification (CAC) [1]. According to the study by Wang F, et al. (2018), CAC is observed in more than 90% of men and in more than 67% of women aged over 70 years [2].

CAC in patients with CAD is associated with complications and unsatisfactory clinical outcomes of percutaneous coronary intervention, even when using new-generation stents [3]. Coronary artery bypass grafting (CABG) is equally effective in patients with simple or complex lesions, bypassing which a new vessel is created. However, in published studies, the authors define severe calcification as an independent predictor of worse outcomes after surgery. Ertelt K, et al. (2013) published a study with a 1-year follow-up period and 755 patients after CABG due to acute coronary syndrome, who were included in the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial. The authors noted that the mortality rates and the incidence of perioperative myocardial infarction (MI) after CABG in patients with CAC were almost 3 times higher than in those without CAC: the one-year mortality rate was 11,8% vs 4,5% (p=0,006), and the prevalence of MI — 31,1% vs 16,4% (p=0,006) [4]. This mortality rate significantly exceeds the general-group level published in the results of modern randomized trials: 3,5% — Surruys PW, et al., SYNTAX trial (2009); 4,2% — Farkouh ME, et al., FREEDOM trial (2012) [5, 6]. Similar results were reported in the study by Bourantas CV, et al. (2015), where patients with severe CAC included in the SYNTAX trial and the SYNTAX CABG registry had a higher 5-year mortality: 17,1% vs 9,9% in the general group (p<0,001), however, differences in the incidence of adverse nonfatal cardiovascular events did not reach significance (26,8% vs 21,8%, p=0,057) [7]. It should be noted that a higher mortality rate, as well as the development of events in groups with CAC, can be interpreted as a result of a more severe comorbidity status (renal failure, hypertension) and multifocal atherosclerosis. Severe CAC was recognized as a significant factor in the increase in mortality and the incidence of cardiovascular events after CABG [4]. The authors note that severe CAC causes technical difficulties in performing distal anastomoses, increases the surgery time length, can lead to vessel wall dissection, distal embolism, and the impossibility of revascularization without endarterectomy; all of these factors may contribute to unsatisfactory outcomes [8].

There are following limitations of the above studies: characterization of calcification was carried out using angiography without the use of highly sensitive methods, such as multislice computed tomography (MSCT) of CA, intravascular ultrasound and optical coherence tomography; the authors did not mention the achievement of complete revascularization; there was no information on the choice of the optimal surgical strategy for the CAC lesions.

The aim was to study the prognostic value of calcification of target coronary arteries (CA) based on the early CABG outcomes in relatively homogeneous groups of patients with complete myocardial revascularization.

Material and methods

The prospective comparative study included 462 patients who underwent elective isolated CABG in the period 2017-2018 at the National Medical Research Center of Cardiology (Russia). Two groups were distinguished: group 1 — patients with TCA calcification (n=108), group 2 — patients without TCA calcification (n=354). The analysis of angiographic data to determine the calcification severity (as well as the assessment of coronary system using the SYNTAX score) was carried out by three independent experts. The target artery was considered calcified if X-ray-positive formations (calcifications) at the level of significant stenoses (occlusions) and distally in the vessel planned for grafting were determined by non-contrast fluoroscopy. In doubtful cases and/or when there was a difference of opinion among experts (in 48 patients), MSCT was performed. In this subgroup, a comparison was made of the diagnostic value of coronary angiography and contrast-enhanced MSCT using a segment involvement score [9]. To assess the coronary bed by segments, the 16-segment American Heart Association classification was used [10]. When the distal diameter was less than the MSCT resolution (<1,5 mm), a vessel- and lesion-specific CAC score was used [11]. Patients with calcification, but without significant coronary artery stenosis, were assigned to group 2.

To reduce the influence of technical factors, CABG was performed in all patients in a standard manner using a cardiopulmonary bypass, cold cardioplegia, and microsurgery. In the vast majority of patients, the left internal thoracic artery was used for myocardial revascularization. In all cases, the tactics of complete revascularization according to the

Characteristics of patients

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Men (%)	79 (73,1%)	270 (76,3%)	NS
Body mass index (M±SD)	28,1±3,5	28±4,2	NS
Age (M±SD)	63,4±7,9	64,5±8,5	NS
Class II angina, n (%) Class III angina, n (%) Class IV angina, n (%)	11 (10,2%) 69 (63,9%) 16 (14,8%)	26 (7,3%) 245 (69,3%) 47 (13,2%)	NS
Unstable angina, n (%)	7 (6,5%)	16 (4,5%)	NS
Silent myocardial ischemia, n (%)	5 (4,6%)	20 (5,7%)	NS
Previous myocardial infarction, n (%)	53 (49,1%)	185 (52,2%)	NS
Ejection fraction, % (M±SD)	57,7±5,3	58,2±7,2	NS
Clinical signs of class >2 HF, n (%)	22 (24,7%)	42 (16,3%)	NS
History of smoking, n (%)	41 (37,9%)	142 (40,1%)	NS
Hypertension, n (%)	92 (85,2%)	268 (75,7%)	NS
Multifocal atherosclerosis, n (%)	47 (43,5%)	92 (25,9%)	<0,05
Diabetes, n (%)	34 (31,5%)	77 (21,7%)	<0,05
CKD ≤3A, n (%)	6 (5,5%)	10 (2,8%)	NS
Previous CVA, n (%)	11 (10,2%)	9 (2,5%)	<0,05
STS score (M±SD)	0,8±0,4	0,7±0,3	NS

Abbreviations: NS — not significant, HF — heart failure, CVA — cerebrovascular accident, CKD — chronic kidney disease.

Preoperative angiographic data

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Three-vessel lesion, n (%)	106 (98,1%)	345 (97,5%)	NS
LCA trunk lesion, n (%)	17 (15,7%)	51 (14,4%)	NS
SYNTAX score (M±SD)	36±3,7	32±3,6	NS
Previous PCI	23 (21,3%)	73 (20,6%)	NS

Abbreviations: NS — not significant, LCA — left coronary artery, PCI — percutaneous coronary intervention.

SYNTAX trial criteria were used, as well as the principle of revascularization of all three main coronary arteries in three-vessel disease [12]. All patients, starting from the first day after surgery, received antiplatelet therapy with acetylsalicylic acid at a dosage of 100 mg. In the case of coronary endarterectomy, anticoagulant therapy was carried out with infusion of unfractionated heparin starting 6-12 hours after surgery and reaching the target values of activated clotting time (150-170 sec), followed by switching to warfarin with the achievement of an international normalized ratio of 2,0-3,0 with a duration of at least 6 months. All patients, without exception, were prescribed statin therapy: most often, atorvastatin 20-80 mg/day and rosuvastatin 10-20 mg/day.

There were following exclusion criteria: a) significantly reduced contractility of the left ventricle (LV) (LV ejection fraction <35%), b) valvular heart disease requiring surgery, c) LV aneurysm, d) previous MI <1,5 months, e) previous heart surgery.

Early outcomes of CABG were evaluated performing the assessment and comparison of intraoperative data, the need for inotropic support and its duration, the incidence of perioperative MI (PMI), mortality, as well as parameters characterizing postoperative recovery. PMI was diagnosed according to the criteria described Fourth Universal Definition of Myocardial Infarction Guidelines [13].

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The medical ethics committee approved this study. All patients signed informed consent.

Statistical processing was performed using the Statistica 10.0 software. With a normal distribution, the variables are presented as mean (M) and standard

Intraoperative characteristics

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Mean revascularization index (M±SD)	4,5±0,8	4,3±0,5	NS
Operating microscope use, n (%)	108 (100%)	354 (100%)	NS
Use of LITA, n (%)	104 (96,3%)	351 (99,1%)	NS
Use of PITA, n (%)	7 (6,5%)	38 (10,7%)	NS
Anastomoses with coronary arteries <1,5 mm in diameter, n (%)	36 (33,3%)	14 (4%)	<0,05
Coronary artery endarterectomy, n (%)	14 (12,9%)	17 (4,8%)	<0,05
Prolonged patch-angioplasty, n (%)	23 (21,3%)	16 (4,5%)	<0,05
Sequential anastomoses, n (%)	15 (13,9%)	26 (7,3%)	<0,05
'Y' grafts, n (%)	35 (32,4%)	44 (12,4%)	<0,05
Myocardial ischemia, min (M±SD)	72±18	59±19	<0,05
CPB duration, min (M±SD)	103±24	90±27	<0,05

Abbreviations: NS — not significant, CPB — Cardiopulmonary bypass, LITA — left internal thoracic artery, RITA — right internal thoracic artery.
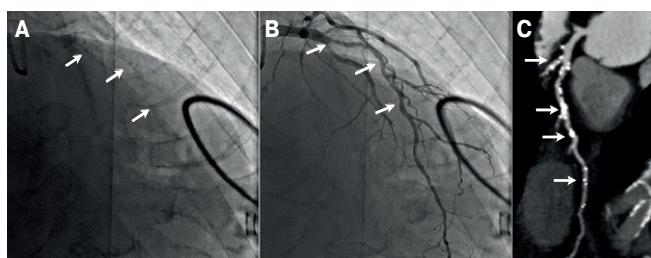

Figure 1 (A, B, C). A. Coronary angiography before contrast enhancement. Arrows indicate calcification in the proximal and middle areas of anterior descending artery (ADA). **B**. Contrast-enhanced coronary angiography. Arrows indicate stenosis in the proximal area and uneven contours in the middle area of ADA. **C**. Multiplanar reconstruction with ADA MSCT. Arrows indicate calcification in the proximal area, pronounced calcification in the middle area, and single calcifications in the distal area of ADA.

deviation (SD). For clinically significant effects, the relative risk and 95% confidence interval (CI) was calculated. To compare two independent groups, the nonparametric Mann-Whitney test was used; to compare the proportions — the chi-squared test or Fisher's exact test. Differences were considered significant at p<0,05.

Results

The mean age of patients in groups 1 and 2 did not differ significantly and amounted to 63,4±7,9 and 64,5±8,5 years, respectively; the vast majority of patients in both groups were men. There were no significant differences between groups for most of the baseline clinical characteristics. However, among patients with calcification, multifocal atherosclerosis, diabetes, and previous cerebrovascular accidents were significantly more frequent. However, the STS score for the risk of surgery were similar in the groups. The demographic and clinical and functional characteristics of the subjects are presented in Table 1.

According to the preoperative coronary angiography (Table 2), multiple CA lesions were noted in all cases. The proportion of patients with left coronary artery stenosis and the SYNTAX score did not differ in the groups. It should be noted that >20% of patients in each group are patients with recurrent angina after percutaneous coronary intervention.

Analysis of the calcification localization showed that, in most cases, calcified lesions were in the three main CAs. The total number of calcified target vessels in 108 patients was 248; in 58 cases, a three-vessel distal lesion was noted. Single vessel calcification was observed in 26 patients; in most cases (n=20), anterior descending artery was involved.

Comparison of diagnostic value of coronary angiography and MSCT in a group of 48 patients who underwent both studies showed that the mean number of detected calcification segments with MSCT is significantly higher than with coronary angiography (8,02±2,6 and 6,02±2, 3, respectively, p<0,05). Figure 1 shows a comparison of images obtained with coronary angiography and MSCT, demonstrating the higher effectiveness of MSCT in detecting distal calcifications.

The frequency of complex surgical interventions in group 1 was higher: 'Y' grafts were used in groups 1 and 2, respectively (odds ratio (OR) 3,4; 95% CI 2,0-5,7; p=0,00005); sequential anastomoses — in 14% (15/108) and 7% (26/354) (OR 2,0; 95% CI 1,0-4,0; p=0,03); prolonged patch-angioplasty — in 21% (23/108) and 5% (16/354) (OR 5,7; 95% CI 2,9-11,3; p=0,0005); anastomoses with arteries <1,5 mm in

Table 4

In-hospital outcomes

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Bleeding (resternotomy), n (%)	4 (3,7%)	14 (3,9%)	NS
Prolonged mechanical ventilation (>24 h), n (%)	2 (1,8%)	5 (1,4%)	NS
Mean length of stay in ICU, days (M±SD)	2,25±0,8	2,1±0,7	NS
Long-term inotropic support (>24 h), n (%)	4 (3,7%)	10 (2,8%)	NS
Perioperative myocardial infarction, n (%)	2 (1,8%)	4 (1,1%)	NS
Transient encephalopathy, n (%)	10 (9,2%)	31 (8,7%)	NS
Cerebrovascular accident, n (%)	2 (1,8%)	3 (0,8)	NS
Heart rhythm disturbances, n (%)	23 (21,3%)	74 (20,9%)	NS
Postoperative length of stay, days (M±SD)	9,7±3,6	8,8±2,4	NS
Hospital mortality, n (%)	0	0	NS

Abbreviations: NS — not significant, ICU — intensive care unit.

diameter — in 33% (36/108) and 4% (14/354) (OR 12,4; 95% CI 6,2-23,7; p=0,00005); coronary endarterectomy — in 17% (18/108) and 5% (16/354) (OR 2,9; 95% CI 1,4-6,2; p=0,003), respectively. As a result, CABG in both groups had an equivalent and sufficiently high revascularization index. The use of complex surgical interventions in group 1 resulted in an increase in cardio-pulmonary bypass duration (103±24 min vs 90±27 min, p<0,05) and myocardial ischemia (72±18 min vs 59±19 min, p<0,05). Despite this, in-hospital outcomes did not show significant intergroup differences. Intraoperative indicators and in-hospital outcomes of the studied groups are presented in Tables 3 and 4. In the postoperative period, all patients received antiplatelet therapy (aspirin), and in the case of endarterectomy — additionally warfarin; all participants also received statins in a dose depending on lipid levels. Adherence to statin (88,9% vs 90,2%, p>0,05) and antiplatelet therapy (95,1% vs 91,7%, p>0,05) did not differ significantly in both groups.

Discussion
In this work, the distal CAC is considered as a problem that requires an individual approach to the diagnosis and determination of surgical tactics. With the specialized techniques for distal anastomoses, we achieved complete revascularization and favorable in-hospital outcomes. The early outcomes of surgery in patients with/without CCA were similar: hospital mortality was not registered; the incidence of bleeding and resternotomy was comparable; the incidence of perioperative MI was similar. All patients who underwent non-fatal perioperative MI were clinically stable by the end of hospitalization. The need for long-term (>24 h) inotropic support, as well as

prolonged (>24 h) mechanical ventilation in the groups was similar. The frequency of arrhythmia, length of stay in the intensive care unit and hospital were similar; there were no cases of in-hospital angina recurrence. Lacunar stroke developed in 2 patients of group 1, in both cases there was an initial neurologic deficit.

Thus, the results obtained indicate that the use of additional surgical techniques in CABG with the complete revascularization in patients with calcified lesions provides the same efficacy and safety as in standard CABG performed in patients with local coronary artery stenosis without calcification. This is at odds with the data demonstrated by Ertelt K, et al. (2013) [4] and Bourantas CV, et al. (2015) [7]. In these studies, calcification was assessed using angiography without the use of MSCT. However, coronary angiography had a higher specificity, but lower sensitivity compared to MSCT in determining CAC. MSCT coronary angiography, being a non-invasive diagnostic method, has both high sensitivity and high specificity for calcification detection. In a relatively small sample (n=48), we noted significantly higher efficacy contrast-enhanced and non-contrast-enhanced MSCT for describing the distal areas of calcified arteries. One way or another, both methods have pros and cons, therefore, in difficult and doubtful cases, we consider it important to use them together. We propose the inclusion of MSCT in the list of necessary tests in cases when an invasive treatment is planned for a patient with CAC.

The current study has a short-term follow-up period. Undoubtedly, further study with the assessment of long-term outcomes is required. The problem as a whole requires a broader consideration: so far, no randomized multicenter trials have been

conducted and there are no practical guidelines for managing this category of patients.

Conclusion

CABG in CAC involves more frequent use of complex reconstructive surgical interventions, endarterectomies, anastomoses with small coronary arteries compared to standard CABG. The complete myocardial revascularization in patients with calcification achieved with these techniques provides in-hospital outcomes similar to those in patients without distal CAC.

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