Review

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The Problem of the Choice of Revascularization in Combined Lesion of the Coronary and Carotid Arteries. Review of Current Recommendations and Article Series

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SUMMARY This article provides data from the current Russian (National guidelines for the management of patients with diseases of the brachiocephalic arteries of 2013; Recommendations "Blockage and stenosis of the carotid artery" of the Ministry of Health of the Russian Federation, 2016) and foreign (European Society of Cardiology / European Society of Vascular Surgeons for Diagnosis and Treatment Peripheral Artery Diseases 2017; Recommendations for myocardial revascularization of the European Society of Cardiology and the European Association of Cardio-Thoracic Surgeons 2018) recommendations regarding the choice of a revascularization strategy for combined coronary and carotid artery disease. Conclusions are drawn about the unresolved issue. A literature review of the largest series of Russian articles by one institution devoted to this topic was carried out. Hospital and long-term outcomes have been demonstrated, as well as predictors of complications for various revascularization strategies. The stages of creation and the results of approbation of a new computer program for risk stratification, which makes it possible to determine the mathematical probability of the development of unfavorable cardiovascular events during the implementation of various surgical tactics, taking into account the individual characteristics of the patient. A conclusion was made about the effectiveness of this development.

Keywords: coronary bypass grafting, carotid endarterectomy, percutaneous coronary intervention, risk stratification, revascularization recommendations, comorbidity, concomitant, restenosis, predictors of complications

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ACVA — acute cerebrovascular accident
ASP — atherosclerotic plaque
CABG — coronary artery bypass grafting
CABS — coronary artery bypass surgery
CEE — carotid endarterectomy
CPB — cardiopulmonary bypass
CS — coronary shunting
ICA — internal carotid artery
EF — ejection fraction
FC — functional class
LV — left ventricle
MFA — multifocal atherosclerosis
MI — myocardial infarction
PCI — percutaneous coronary intervention
TIA — transient ischemic attack

INTRODUCTION

The problem of choosing a revascularization strategy for combined atherosclerotic lesions of the coronary and carotid arteries has not yet been fully resolved. The lack of a sufficient number of randomized trials and the uncertainty in the current recommendations practically exclude the conditions for the formation of a mediator capable of resolving this issue [1–5].

OVERVIEW OF CURRENT RUSSIAN AND FOREIGN RECOMMENDATIONS

The 2013 National Guidelines for the Management of Patients with Brachiocephalic Artery Disease states that prior to myocardial revascularization, “it is advisable to treat stenosis of the internal carotid artery (ICA) as a first step”[6]. However, despite this, the authors provide data from a large meta-analysis, which included 8972 simultaneous and staged operations [7]. The results of the study demonstrate that both tactics of surgical correction are associated with a comparable combined risk (death + myocardial infarction (MI) + stroke), reaching 10–12% [7].

However, for what reason revascularization is staged the first choice strategy in the recommendations when carotid endarterectomy (CEE) is initially performed? There is no explanation for this question. Moreover, in the next paragraph, the authors refute this conclusion, arguing that there can be no single approach to the treatment of patients with simultaneous lesions of both pools, and the surgical correction strategy should be chosen individually, taking into account the stratification of the risk of complications and the experience of the medical institution. [6]. The place of combined intervention on the coronary and carotid arteries is also unclear, although this tactic has been in the area of special attention of the scientific community in recent years [8–12]. In addition, if symptomatic myocardial damage and asymptomatic carotid stenosis are diagnosed, then the logic in the priority CEE, according to the recommendations, is not clear.

The clinical guidelines "Occlusion and stenosis of the carotid artery" of the Ministry of Health of the Russian Federation, adopted in 2016, also demonstrate the conclusion that it is advisable to perform CEA first and only the second stage of myocardial revascularization (level of persuasiveness of recommendations - B, level of evidence 2a)[13]. At the same time, an important comment is made to the postulate that the choice of

treatment strategy should be only individual, based on the level of stratification of the risk of complications and the experience of the medical institution [13].

The 2017 European Society of Cardiology/European Society of Vascular Surgeons guidelines for the diagnosis and treatment of peripheral arterial disease state that there is insufficient evidence for the need for first-stage CEA in patients with asymptomatic ICA stenosis who are about to undergo coronary bypass grafting (CABG) [14]. This strategy is not recommended as the only correct one, even in the presence of 70-99% stenosis of the ICA (Class III, Level of Evidence B), but the presence of bilateral hemodynamically significant lesions/contralateral occlusion is an exception (Class IIb, Level of Evidence B) [14]. If this or any other tactic is necessary, then it should be approved only by a multidisciplinary council (Class I, Level of Evidence C) [14]. In a randomized trial, which immediately gives recommendations, in the presence of asymptomatic ICA stenosis, the most effective and safe are staged CEE revascularization followed by CS (CEE-CABG) and simultaneous CEA + CABG. In turn, staged CS-CEE is associated with the highest risk of adverse cardiovascular events (8.8% relatively 1.0%, p=0.02) [15]. According to the authors of the recommendations, the most important criterion for a first-stage reconstructive intervention on the ICA is the presence of a hemodynamically significant (50–99%) symptomatic atherosclerotic plaque (ASP), since these patients have the greatest number of acute cerebrovascular accidents/transient ischemic attacks (ACVA /TIA) after CABG (class IIa, level of evidence B) [14]. Thus, none of the above postulates has level A evidence (data from numerous randomized clinical trials and meta-analyses), and only one conclusion characterizes the highest class I (it has been proven that this type of treatment or diagnosis is useful and effective; recommended / indicated) — about the need to choose a revascularization strategy by a multidisciplinary council [14].

In 2018, recommendations for myocardial revascularization by the European Society of Cardiology and the European Association of Cardiothoracic Surgeons were published [16]. However, no new conclusions were made, the authors duplicated the conclusions of the recommendations of the European Society of Cardiology / European Society of Vascular Surgeons for the diagnosis and treatment of peripheral arterial disease in 2017 [14, 16].

Thus, the current domestic and foreign recommendations do not provide a definitive answer to the question of which revascularization strategy is most effective in combined coronary and carotid lesions [7, 13, 14, 16].

The place of the simultaneous CEE+CS in solving this problem remains unclear. Only a few final decisions are known - the choice of treatment tactics should be carried out by a multidisciplinary commission based on risk stratification of the level of complications and only personalized. There is no single universal surgical treatment strategy. Attempts to study this problem are most often limited to an analysis of the causes and frequency of postoperative adverse events, a comparison of the level of complications after a particular revascularization technique [17–21]. However, in 2016, a group of domestic authors founded a large-scale study to solve the problem of choosing a method of revascularization in patients with simultaneous atherosclerotic lesions of the coronary and carotid arteries.

Aim of this work was a review of the largest domestic series of articles devoted to solving the problem of choosing a revascularization strategy for combined atherosclerotic lesions of the coronary and carotid arteries.

REVIEW OF THE LARGEST SERIES OF PUBLICATIONS BY THE LEADING GROUP OF RUSSIAN AUTHORS

Due to the fact that the study (conducted under the leadership of the hero of Kuzbass L.S. Barbarash), which will be discussed, was many years old and consisted of a series of articles, the authors did not publish the general design of the entire work. Thus, we summarized the entire body of literature and drew up a plan that included several points (Fig. 1). At the first stage, a sample of 330 patients with simultaneous atherosclerotic lesions of the coronary and carotid arteries was retrospectively formed. Depending on the implemented revascularization strategy, all patients were divided into four groups: staged CABG–CEE (n=104), combined CABG+CEA (n=116), hybrid PCI (percutaneous coronary intervention) + CEA (n=64), and staged CEE-CS (n=46). We studied hospital and long-term results of operations, as well as predictors of adverse events at all stages of observation [22, 23]. Further, thanks to the use of mathematical data processing (calculation of prognostic coefficients and integral indicators), a program was created to stratify the risk of complications and select the optimal tactics of surgical treatment (see Fig. 1). Each of the groups of patients was assessed using two prognostic scales EuroScore II (severity of concomitant pathology, severity of clinical

status and risk of surgical complications) (URL: http://www.euroscore.org/calc) and SYNTAX Score (severity of coronary atherosclerosis) (URL: http://www.rnoik.ru/files/syntax). The choice of surgical treatment strategy was carried out by a multidisciplinary team (cardiovascular surgeon, endovascular surgeon, neurosurgeon, cardiologist, neurologist, resuscitator, anesthesiologist). The following endpoints were studied in the work: death, MI, stroke/TIA, repeated unplanned revascularization, clinically significant bleeding according to the Bleeding Academic Research Consortium (BARC), combined endpoint (death+stroke/TIA+MI) [22, 23].

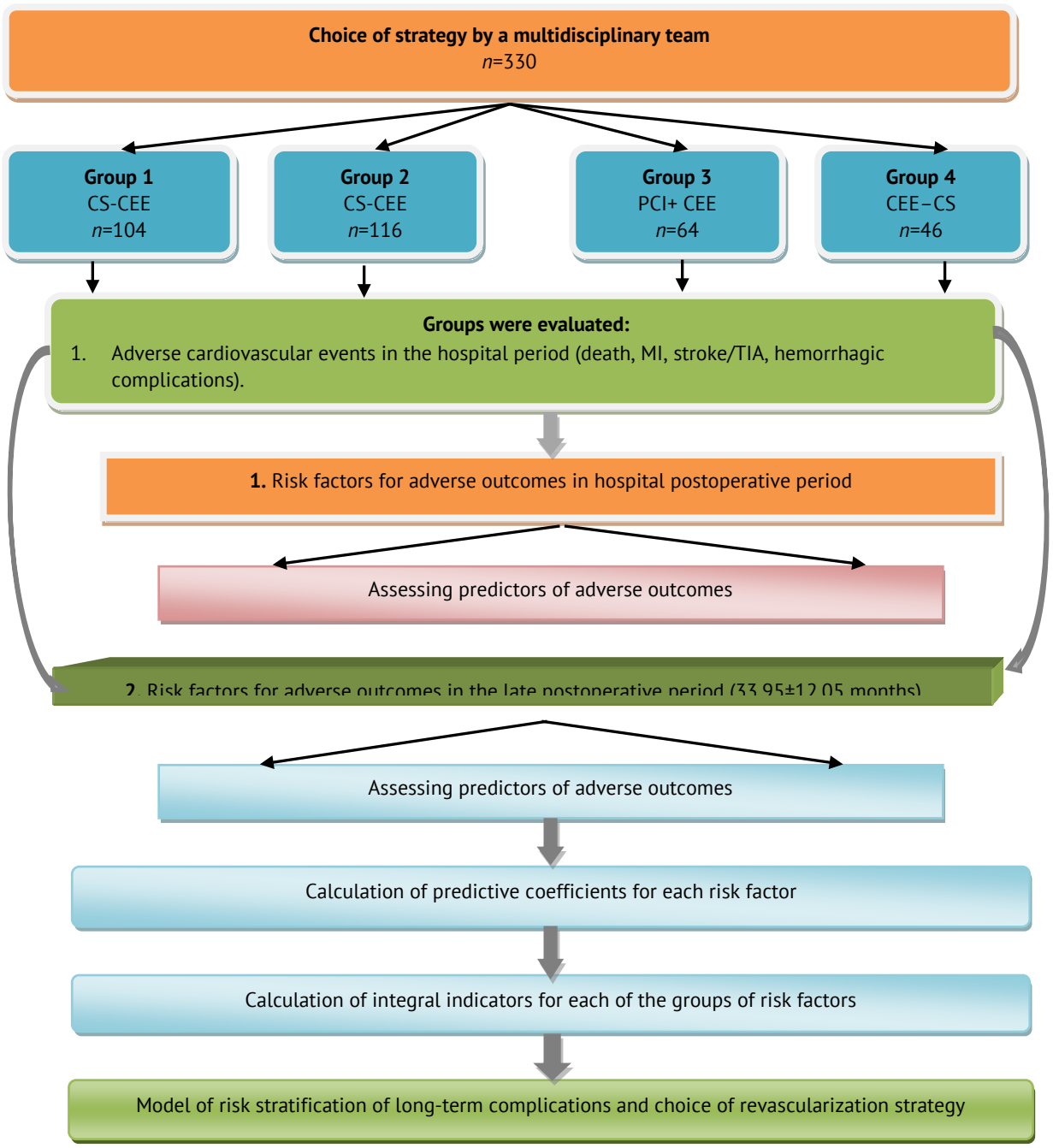

Fig. 1. Study design.

The authors found that death, MI, stroke/TIA and hemorrhagic complications were most often observed in the CABG + CEE group. Thus, the combined end point reached the highest values in the CS+CEE group. In patients after the implementation of the revascularization strategies PCI + CEE and CEE-CS, only hemorrhagic complications were noted (Table. 1) [22, 23]. The authors deliberately did not use statistical methods to compare the results of the operation. They attributed this step to the fact that in the vast majority of clinical, demographic and angiographic parameters using standard statistical methods (Pearson Chi-square, Mann-Whitney, Kruskle-Wallis) the groups were not comparable. Thus, the only legitimate way to compare the results of operations was to bring the groups to a "common denominator." The most common statistical method to achieve this condition is propensity score matching. However, its use would reduce the already small groups of PCI + CEE (n=64) and CEE-CS (n=46). In addition, the goal of the authors was not to compare the methods of operations, but to analyze the specific results after each method of revascularization, identify predictors of complications and, based on complex mathematical analysis, create a program for risk stratification and choice of treatment strategy. Therefore, as part of their work, in order to avoid violating the laws of statistics, the authors limited themselves to an arithmetic comparison of the % of endpoint cases between groups.

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Table 1

Hospital outcomes

Indicators	CS–CEE		CS+CEE		PCI+CEE		CEE–CS	
	n	%	n	%	n	%	n	%
Death	1	0.96	2	1.72	0	0	0	0
Myocardial infarction (non-fatal)	1	0.96	2	1.72	0	0	0	0
ACVA/TIA (non-fatal)	3	2.88	5	4.31	0	0	0	0
Hemorrhagic complications	3	2.88	9	7.75	3	4,68	1	2,17
Combined endpoint (death+MI+ACVA/TIA)	5	4.8	9	7.75	0	0	0	0

Notes: * — death (from MI and stroke) + MI + stroke/TIA + repeated revascularization. MI - myocardial infarction; CS — coronary bypass grafting; CEE - carotid endarterectomy; ACVA - acute cerebrovascular accident; TIA - transient ischemic attack.

In the long-term follow-up period (33.95±12.05 months), death from cardiovascular events in a greater percentage of cases was detected in the CS-CEE and PCI + CEE group. Isolated cases of MI were identified among patients after CS + CEA and PCI + CEA. The largest number of stroke/TIA was also noted after PCI + CEA (Table. 2) [22, 23].

Table 2

Long-term results

Indicators	CS–CEE		CS+CEE		PCI+CEE		CEE–CS	
	n	%	n	%	n	%	n	%
Death	14	14.3	12	11.7	9	16.6	5	11.9
Myocardial infarction (non-fatal)	0	0	1	0.98	1	1.8	0	0
ACVA/TIA (non-fatal)	3	3	4	3.9	6	11.1	1	2.4
Combined endpoint *	16	16.3	17	16.6	16	29.6	6	14.3

Notes: * — death (from MI and stroke) + MI + stroke / TIA + repeated revascularization. MI - myocardial infarction; CS — coronary bypass grafting; CEE - carotid endarterectomy; ACVA - acute cerebrovascular accident; TIA - transient ischemic attack.

The next step was to study the risk factors for the development of complications in the hospital and long-term periods in the general sample, as well as after each strategy and type of operation, using binary logistic regression with stepwise inclusion and exclusion of predictors.

When analyzing risk factors for the development of adverse events after CEE, the presence of a large number of cardiac predictors at all stages of observation attracts attention (Table 3). And if in the hospital period it is only angina pectoris II-III functional class (FC), then in the medium-term - also the average severity of atherosclerotic lesions of the coronary bed according to SYNTAX Score, and in the distant period - a severe defeat [24–27]. In addition, in the long-term follow-up period, a reduced ejection fraction (EF), left ventricular (LV) aneurysm, and a history of CS are added (probably due to shunt occlusion and progression of angina pectoris) [27]. This combination of predictors along with a pronounced comorbid background (EuroSCORE II at least 3%) reflects, first of all, the severity of the patient and the high risk of adverse cardiovascular events [27].

Table 3

Predictors of complications aftercarotid endarterectomy

Hospital period		
Female gender	1.6805	1.0358–2.7265
Angina pectoris II–III FC	1.6734	1.0532–2.6588
MFA with hemodynamically significant lesion of 3 arterial pools	2.2381	1.1847–4.2281
Combined PCI + CEE	2.7180	1.2503–5.9082
Mid-term period		
Angina pectoris II–III FC	3.8	1.2–11.9
SYNTAX score at least 22	2.83	1.137–7.086
Remote period		
Unstable plaque in non-operated ICA	2.1272	1.1759–3.8479
Opposite ICA occlusion	3.0690	1.8019–5.2271
Decreased LVEF less than 39%	2.0007	1.2297–3.,2552
SYNTAX score at least 33 (high risk)	2.1288	1.3476–3.3628
Clamping for more than 40 minutes	2.9407	1.1825–7.3129
History of CS or MABG	1.8680	1.2008–2.9060
LV aneurysm	5.4533	1.3811–21.5330
MFA with hemodynamically significant lesion of 3 arterial pools	2.4360	1.0816–5.4867
EuroSCORE II at least 3%	17.0743	4.7958–60.7890

Notes: CS — coronary artery bypass grafting; ICA - internal carotid artery; LV - left ventricle; MCSH - mammary-coronary shunting; MFA - multifocal atherosclerosis; EF - ejection fraction; FK - functional class; PCI - percutaneous coronary intervention.

Thus, staged CEE followed by CS will always be accompanied by an increased risk of adverse coronary events in the interval between stages. In addition, it should be noted that in the long-term follow-up period, such cerebrovascular risk factors as contralateral occlusion and unstable ASP in the contralateral ICA are added. The authors attribute this to the absence of patients at the second stage of revascularization — CEE on the opposite side and low compliance of patients [25–28]. Also noteworthy is such a predictor as prolonged clamping of the ICA during CEE. On the one hand, it is not clear what is the relationship between the intraoperative feature of the intervention and the long-term result. However, the explanation is as follows. If during the execution of the vascular suture and the start of blood flow, the suture eruption occurs, bleeding from the anastomosis, this event requires the imposition of secondary sutures, which can often result in a narrowing of the lumen of the vessel and a violation of the hemodynamic flow [27–29]. This, in turn, will lead to restenosis of the reconstruction zone through neointimal hyperplasia, which can cause the development of stroke/TIA in the long-term follow-up period. Thus, prolonged clamping of the ICA may demonstrate technical difficulties during CEE [27, 29, 30].

Among the predictors of the development of complications in the groups of combined, hybrid and staged surgery in the hospital period, several groups of factors are also determined. Of these, the III-IV FC of angina pectoris belongs to the cardiovascular ones, demonstrating the severity of coronary atherosclerosis [31, 32]. In the cerebrovascular group, various variants of ipsi- and contralateral lesions of the ICA are distinguished, as well as the viability of the circle of Willis, which was studied for the first time in world practice. Thus, the severity of stenosis of the unoperated ICA, the presence of an open configuration of the circle of Willis significantly reduce the compensatory capabilities of cerebral collateral circulation during arterial clamping during CEE, which can provoke the development of an ischemic catastrophe in the brain [31, 32].

Among the risk factors, the authors also highlight some comorbid pathology: chronic renal failure, a history of ischemic stroke, chronic cerebral ischemia of stage II, which, along with EuroSCORE at least 3, reflects the severity of the patient's condition [31–33]. The authors also drew attention to the fact that in the CEE + CS and CEE-CS group, the maximum number of patients with a severe comorbid background was concentrated. Thus, the analysis showed that the use of these revascularization strategies in itself became a risk factor for the development of complications [31, 32]. Separately, among the predictors of hospital accidents, perioperative characteristics are distinguished, among which are: prolonged cardiopulmonary bypass (CPB) and bleeding [31, 32]. By analogy with prolonged clamping of the ICA (Table 3), the authors explain the role of these factors as reflecting the technical difficulties of the intraoperative stage: possible multivessel coronary artery disease requiring implantation of three or more shunts, additional sutures in the anastomosis area due to bleeding, etc. (Table 4) [31, 32].

n the long-term follow-up period, two types of risk factors were identified. Perioperative factors included bleeding, prolonged clamping of the ICA, and the presence of more than four cardioplegias. The influence of these predictors on long-term outcomes was explained by the authors by analogy with the same group during the hospital period — the technical difficulties of the operation [23]. Cardiovascular risk factors were as follows: reduced LV EF and multivessel coronary lesion in combination with hemodynamically significant stenosis of the left coronary artery trunk. These conditions in the development of shunt dysfunction, progression of atherosclerosis can contribute to decompensation of coronary hemodynamics with the formation of MI and death [23].

At the next stage of their study, the authors conducted a complex mathematical analysis: they calculated prognostic coefficients for each risk factor, which reflected the likelihood of developing a complication in the presence of this condition [34, 35]. Further, having divided them into three groups (clinical-demographic, coronary and cerebrovascular ones), integral indicators were calculated - values that reflect the complex contribution of this cohort of factors to the formation of an adverse cardiovascular event at the hospital and long-term stages of observation [36, 37]. After conducting a regression analysis and determining those integral indicators that have a significant impact on the outcomes of each revascularization strategy separately, the authors created logistic models for each of the four studied treatment tactics [36,37,38]. On the basis of the obtained data, a computer program and a mobile phone program were created that can personalize, taking into account the patient's individual indicators, calculate the numerical probability of developing complications, determine the prognosis and risk of possible adverse outcomes [39,40].

Table 4

Predictors of complications after combined, hybrid and staged revascularization strategies

Variable	Odds ratio	95% confidence interval
Hospital period		
III-IV FC angina pectoris	34.7653	5.4385–222.2336
Bleeding from 3 points on a scale BARC	90.5695	11.6916–701.6014
Chronic renal failure	31.2114	3.9081–249.2625
Sequential CEE-CS	3.3042	1.3677–7.9826
One-stage CEE + CS	5.9541	3.1240–11.3481
History of TIA or stroke	6.8222	1.0418–44.6763
AC for 74 minutes or less	0.4677	0.2338–0.9355
Scale score EuroSCORE from 2 or less	0.2812	0.0920–0.8595
Elderly age	3.621	1.740–7.538
EuroSCORE at least 3	4.365	1.534–12.42
Chronic cerebral ischemia II	4.253	2.264–7.988
Vicious circle of Willis	0.335	0.203–0.552
Degree of stenosis of the ipsilateral ICA: 90– 99%	2.764	1.618–4.721
Unstable plaque in the ipsilateral ICA	1.742	1.067–2.844
Degree of ICA stenosis with contralateral ICA: 90–100%	16.558	8.872–30.902
Remote period		
Number of cardioplegias more than 4	3.4909	1.4488–8.4115
Clamping the ICA for 30 minutes or more	2.3575	1.0376–5.3565
Bleeding of 2 points or more on the scale BARK	2.0293	1.1598–3.5506
Ejection fraction less 50%	4.4351	1.3136–14.9739
Damage to the trunk of the left coronary artery and more than three additional coronary arteries	2.6721	1.2762–5.5952

Notes: CS — coronary artery bypass grafting; ICA – internal carotid artery; CPB - cardiopulmonary bypass; CEE - carotid endarterectomy; ACVA - acute cerebrovascular accident; TIA - transient ischemic attack; FC - functional class.

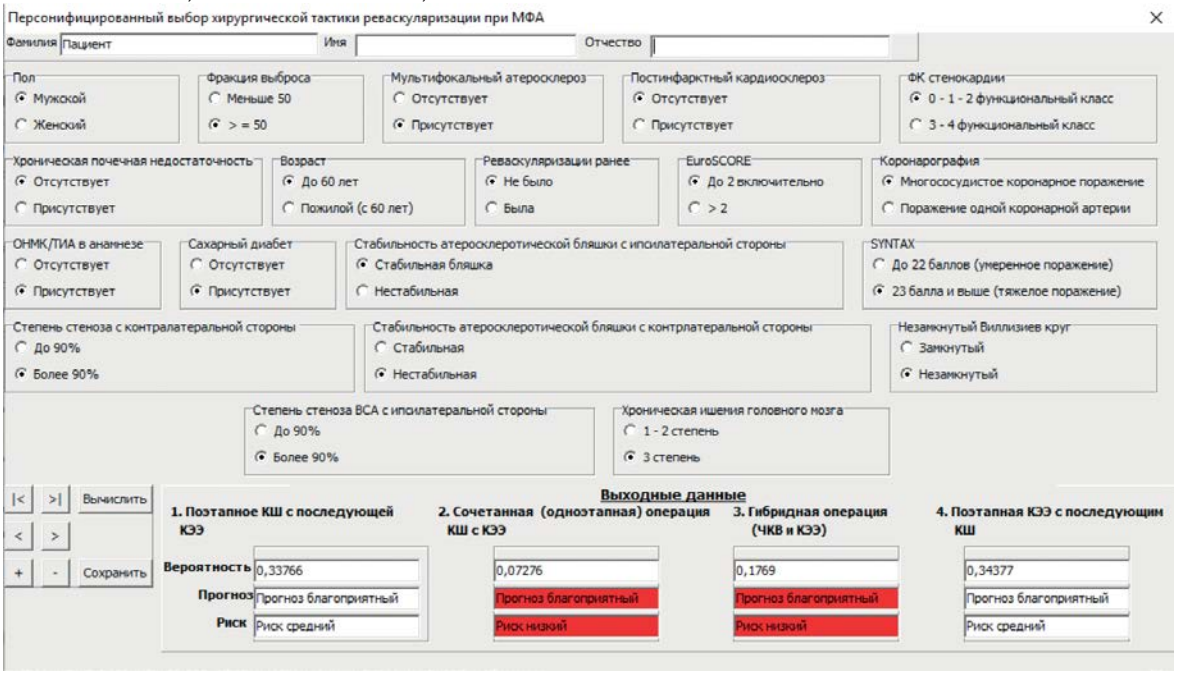

Fig. 2. Computer program interface

Notes: КШ — coronary artery bypass grafting; КЭЭ — carotid endarterectomy; ОНМК — acute cerebrovascular accident; ТИА — transient ischemic attack; ФК — functional class; ЧКВ — percutaneous coronary intervention

The next step required prospective testing of the program in clinical practice, which lasted from 2017 to 2019. It was used in determining the revascularization strategy by a multidisciplinary commission [41–43]. Thus, this mathematical development has become an additional tool in the arsenal of methods for choosing surgical correction. In the overwhelming majority of cases, when the multidisciplinary commission decided in favor of implementing the treatment strategy that the program did not offer, complications developed in the postoperative period [42–44]. In all cases, when the calculation of the program and the decision of the commission coincided, a satisfactory outcome of revascularization was obtained [42–44]. The effectiveness of the development was also proven on the example of complex clinical cases: in the combination of coronary and carotid stenosis in combination with rupture of intracerebral arterial aneurysm; with critical stenosis of the vertebral artery, as well as multiple occlusive-stenotic lesions of the brachiocephalic arteries [45–48].

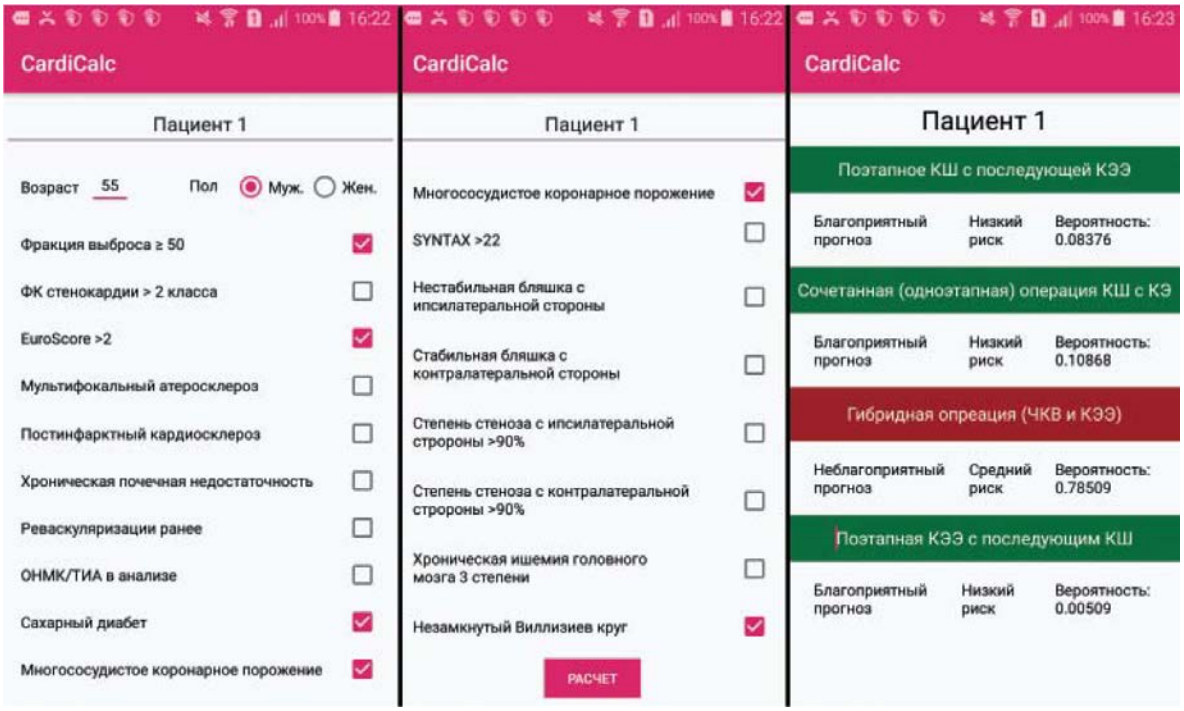

Fig. 3. Mobile phone program interface

Notes: КШ — coronary artery bypass grafting; КЭЭ — carotid endarterectomy; ОНМК — acute cerebrovascular accident; ТИА — transient ischemic attack; ФК — functional class; ЧКВ — percutaneous coronary intervention

CONCLUSION

The issues of choosing a revascularization strategy for simultaneous atherosclerotic lesions of the coronary and carotid arteries will be fully resolved when there is certainty in the current recommendations. To date, only three undeniable statements are known: treatment tactics should be determined personally, by a multidisciplinary commission, based on the stratification of the risk of complications. The presented series of articles demonstrated the stages of creating a mathematical model and a program for a computer and a mobile phone. From the analysis of the results of revascularization in 2016, the identification of predictors of complications, we followed the entire path of creating the program, including its testing in clinical practice since 2019. The results of testing confirm the effectiveness of this development. Thus, it can be accepted as an additional tool in the arsenal of methods for choosing a revascularization strategy, set by Russian and foreign recommendations.

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