Software for Optimal Sequencing of Endovascular Correction of Three-Vessel Coronary Disease in Patients with Acute Myocardial Ischemia

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Selection of inadequate algorithm for endovascular correction of three-vessel coronary disease leads to an increase in the number of adverse cardiac events in patients with acute myocardial ischemia.

The aim of the study is to evaluate the efficacy of the developed software for optimal sequencing of correction of three affected coronary territories in patients with acute myocardial ischemia and three-vessel coronary disease.

Materials and Methods. Treatment results were evaluated in 101 patients with acute coronary syndrome (ACS). Correlation analysis was performed in all patients to determine the sequence of correction for three affected coronary territories as proposed by the operating surgeon, three independent experts or recommended by the developed computer programs "Sapphire 2015 — Right dominance" and "Sapphire 2015 — Left dominance".

Results. Exact similarity in endovascular correction strategies proposed by the software and experts was observed in 72 patients (71.3%); partial similarity — in 28 (27.7%); total difference — in 1 patient (1.0%) (n=101; R=0.864; τ=0.822; p=0.000002). Exact similarity in endovascular correction strategies offered by the software and the operating surgeon was observed in 39 patients (38.7%); partial similarity — in 55 (54.5%); total difference — in 7 (6.9%) (n=101; R=0.836; τ=0.677; p=0.000001). However, early postoperative mortality was reported in those ACS patients for whom there was selected non-optimal sequence of correcting three affected coronary territories during the intervention as recommended by the software.

Conclusion. It is reasonable to use the developed software "Sapphire 2015 — Right dominance" and "Sapphire 2015 — Left dominance" to select the optimal sequence for correction of three-vessel coronary disease in patients with ACS.

Key words: acute coronary syndrome; three-vessel disease; endovascular intervention; revascularization sequence; surgical strategy.

Introduction

The high percentage of revealing three-vessel coronary disease in patients with acute coronary syndrome (ACS) makes it necessary to search for optimal strategy of endovascular surgery in such patients [1, 2]. However, appropriateness of performing complete endovascular myocardial revascularization in patients with ACS and three-vessel coronary disease has been no final and irrefutable dogma so far [3]. Today, surgeons tend to refuse from using "incomplete myocardial revascularization" concept in patients with ACS after correction of clinically relevant coronary artery disease. The term "staged revascularization" is increasingly used in literary sources [4].

It should be noted that the approach to performing staged revascularization involves appropriate sequencing of correction of the affected coronary bed and particular attention should be paid not only to the correction of vessels in the clinically relevant territory, but also to the staged endovascular stenting of related coronary arteries affected by the disease [5]. It is important to emphasize that selection of inadequate algorithm for endovascular correction of three-vessel coronary disease contributes to an increase in the number of major adverse cardiac events to 36.7% [5]. In the literature available, we have found no optimal, sufficiently convenient, effective and efficient algorithms for sequencing of endovascular correction of three-vessel hemodynamically significant atherosclerotic coronary disease in patients with ACS.

The aim of the study is to evaluate the efficacy of the developed software for optimal sequencing of correction of three affected coronary territories in patients with

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acute myocardial ischemia and three-vessel coronary disease.

Materials and Methods

The study involved evaluation of treatment results in 101 patients with ST-elevation acute coronary syndrome (STE-ACS) and non-ST-elevation acute coronary syndrome (NSTE-ACS), who were admitted to Nizhny Novgorod City Clinical Hospital No.5 in the period from February 2016 to April 2019. The patients included 45 males (44.6%) and 56 females (55.4%), the mean age was 63.6±22.8 years (41 to 86 years). The study complies with the Declaration of Helsinki (2013) and was performed following approval by the ethic committee of Privolzhsky Research Medical University. Written informed consent was obtained from every patient.

Clinically significant acute ischemia was diagnosed in the anterior and anterolateral walls of the left ventricle in most cases (Table 1).

Hospital mortality risk and myocardial infarction probability were stratified using the TIMI Score (for STE-ACS patients) and the GRACE Score (for NSTE-ACS patients). A high risk of in-hospital mortality (the TIMI Score of more than 8 points) was reported in 34 of 59 STE-ACS patients (57.6%).

The average TIMI Score in STE-ACS patients was 5.9±3.3 points. A high risk of in-hospital mortality and myocardial infarction development (the GRACE Score of >140 points) was reported in 36 of 42 (85.7%) NSTE-ACS patients under observation. The average GRACE Score was 203.7±40.7 points in NSTE-ACS patients. The severity of coronary disease was calculated using the SYNTAX Score calculator software, v. 2.11. The average score for STE-ACS patients was 28.2±12.9, 31.3±19.3 for NSTE-ACS patients.

Table 1

Characterization of patients with acute coronary syndrome

Clinical features of acute coronary syndrome	Number of patients	
	Absolute number	%
Clinical forms of acute coronary syndrome:		
ST-elevation	59	58.4
non-ST-elevation	42	41.6
Localization of clinically relevant left ventricular ischemia:		
the anterior wall	30	29.7
the anterolateral wall	10	9.9
the posterior wall	32	31.7
the posterolateral wall	9	8.9
the lateral wall	8	7.9
the anterior and lateral walls	8	7.9
the anterior and posterior walls	3	3.0
circular ischemia	1	1.0

The clinical picture of coronary heart disease was diverse in patients under observation prior to hospitalization for ACS. Within 1 month before the onset of acute myocardial ischemia, 35 patients (34.7%) were diagnosed with progressive angina, 23 (22.8%) had primary angina pectoris. 15 patients (14.8%) had no significant coronary history. During 12 months prior to ACS manifestations, 28 patients (27.7%) had stable effort angina classified mainly as FC III according to the Canadian Cardiovascular Society grading system.

Previous myocardial infarctions were reported in 39 of 101 patients (38.6%): non-Q-wave infarction was revealed in 23 cases (22.8%), Q-wave infarction — in 16 cases (15.8%). Most of those examined — 28 out of 39 (74%) — had one myocardial infarction in previous history, 2 infarctions were reported in 8 patients (21%), 3 infarctions — in 3 persons (5%).

Important inclusion criteria for participation of patients in our study were the presence of ACS with clear electrocardiographic signs of ST segment elevation or depression (the J-point shift of 2 cm above or below the isoline in at least two chest leads); three-vessel atherosclerotic coronary disease. During selective coronary angiography, at least one significant lesion (stenosis of more than 50%) was visualized in the left anterior descending artery (LAD), the circumflex artery (CA) and the right coronary artery (RCA) territories in all patients. Patients with chronic occlusions, single- and two-vessel coronary disease, as well as patients with a history of coronary artery bypass grafting were excluded from our study.

After selective coronary angiography, STE-ACS patients underwent urgent endovascular correction of complex three-vessel atherosclerotic coronary disease as part of an early invasive strategy. The average door-to-balloon time in our study was 71.2±8.7 min.

High-risk NSTE-ACS patients underwent endovascular surgery within the first 24 h of hospital admission as part of an early invasive strategy.

During percutaneous coronary intervention (PCI), complete endovascular surgical revascularization of the myocardium was performed in 31 patients (30.7%), incomplete revascularization — in 63 (62.4%). Seven patients (6.9%) were recommended to undergo emergency coronary bypass surgery.

The sequence of endovascular correction of coronary blood flow performed during PCI was determined using “Sapphire 2015 — Right dominance” computer program (software registration certificate No.2016618262 dated July 26, 2016) and “Sapphire 2015 — Left dominance” program (software registration certificate No.2016617353 dated July 1, 2016), specifically developed at the Department of X-ray Endovascular Diagnosis of Privolzhsky Research Medical University (Nizhny Novgorod).

The codes of both programs are based on the principles of changes in coronary hemodynamics, identified by the specialists of A.N. Bakulev Scientific

Center for Cardiovascular Surgery in patients with stable coronary artery disease depending on the disease severity [6]. Taking into consideration the specific changes in the coronary hemodynamics of patients with coronary atherosclerosis, we have introduced additional coefficients to adjust the Center's technique for patients with acute myocardial ischemia, which is reflected in the program code written by us.

The program-simulated sequence of endovascular coronary correction was compared with the endovascular surgery strategy selected by the operating surgeon, as well as with the analysis of revascularization strategy conducted by three independent experts. The advisory decision was considered as reference for our study only if the opinion of all three experts regarding the intervention strategy in the group of patients under study was exactly similar.

Patient survival rate was analyzed in the early postoperative period (up to day 20 after the intervention).

Statistical data processing was performed using Statistica 10.0 software. The results were presented as M±SD, where M is mean value, SD is standard deviation of the standard error. The Spearman rank correlation coefficient (R) was used to analyze the results and the Kendall t-test was used to compare two independent variables [7]. The differences were considered statistically significant at $p<0.01$.

Results

Analyzing recommendations of "Sapphire 201 — Right dominance" and "Sapphire 2015 — Left dominance" programs and opinions given by three independent experts on possible sequences of stenting the three affected coronary territories necessary for patients under study, we found that exact similarity of the proposed endovascular correction strategies was reported in 72 (71.3%) patients; partial similarity — in 28 (27.7%) (n=101; R=0.864; τ=0.822; p=0.000002). Total difference between the used and proposed sequence of correction of three coronary territories was observed in one subject (Figure 1 (a)).

Correlation analysis of priorities in the stages of the LAD territory correction based on the recommendations given by the software and three independent experts showed that there was exact similarity in the opinions of artificial intelligence and natural intelligence in 89 cases (88.1%) (n=101; R=0.888; p=0.000002).

In correlation analysis of priorities in the stages of the CA territory correction, the exact similarity in the opinions of artificial intelligence and natural intelligence was observed in 82 cases (81.1%) (n=101; R=0.729; p=0.000004), and in 86 cases for RCA territory (85.1%) (n=101; R=0.897; p=0.000001).

Analyzing the recommendations of computer programs and the opinion of the operating surgeon on the appropriate sequence of stenting the three coronary territories (LAD, CA, and RCA), we found that exact similarity of the proposed endovascular correction strategies was observed in 39 cases (38.7%); partial similarity — in 55 (54.4%) (n=101; R=0.836; τ=0.677; p=0.000001). Total difference in correction sequences for the three coronary territories was observed in 7 cases (6.9%) (Figure 1 (b)).

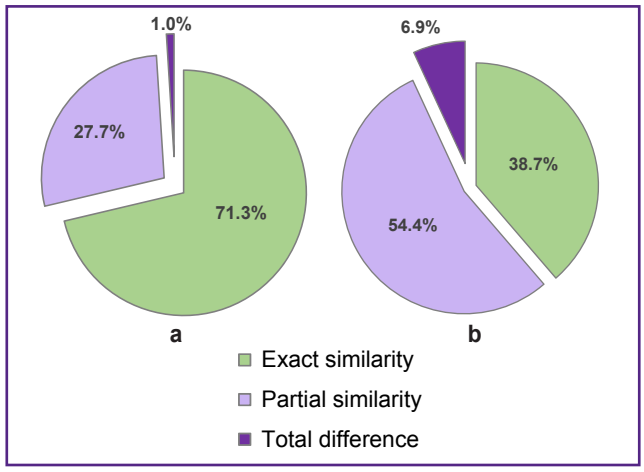

Figure 1. Similarity and difference in endovascular correction strategies in all patients under study:
(a) as recommended by computer programs and three independent experts (R=0.864; p=0.000002); (b) as recommended by computer programs and the operating surgeon (R=0.836; p=0.000001)

Correlation analysis of priorities in the stages of the LAD territory correction based on the recommendations given by the software and the operating surgeon showed that the exact similarity in the opinions of artificial intelligence and natural intelligence was observed in 58 cases (57.4%) (n=101; R=0.722; p=0.000003).

Computer programs regarded the LAD territory correction as the first-priority task in 39 cases (38.7%), the surgeon's opinion was the same in 23 cases (22.7%). It was recommended by artificial and natural intelligence to perform the LAD territory correction on a second-priority basis during PCI for ACS in 30 (29.7%) and 8 (7.9%) patients, respectively. Stenting of LAD and its major branches on a third-priority basis (at the final stage of PCI or repeated intervention during the next hospitalization) was recommended by computer programs in 32 (31.7%) and in 62 (61.4%) cases by the surgeon (Figure 2 (a)).

Correlation analysis of priorities in the stages of the CA territory correction proposed by the computer programs and the operating surgeon showed that there was exact similarity in the opinions of artificial intelligence and natural intelligence in 73 cases (72.3%) (n=101; R=0.667; p=0.000076).

Computer programs regarded the CA territory correction as the first-priority task in 17 cases (16.8%), the surgeon — in 18 cases (17.8%). It was recommended by artificial and natural intelligence to perform the CA territory correction on a second-priority

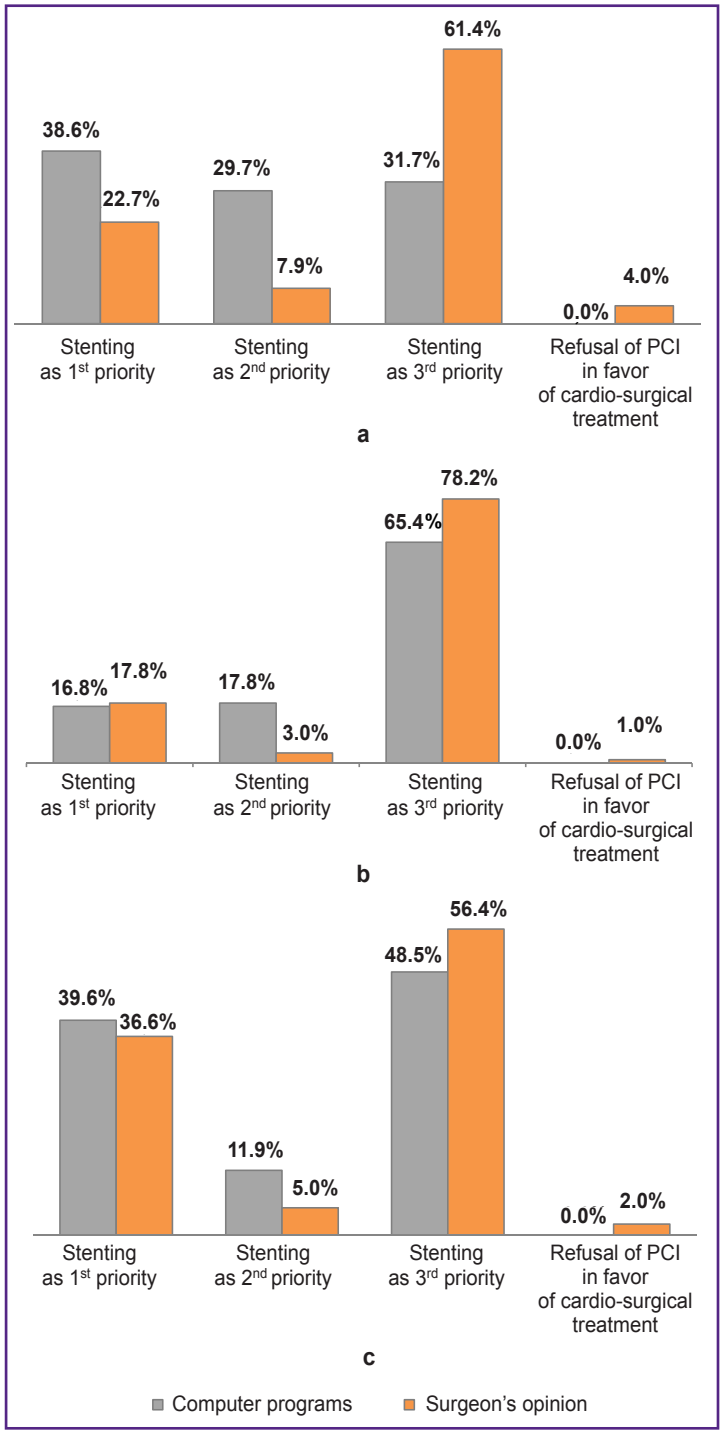

Figure 2. Correlation analysis of recommendations given by computer programs and opinions of the operating surgeon on the sequence of repairing the affected coronary territories:
(a) the LAD territory (R=0.722; p=0.000003); (b) the CA territory (R=0.667; p=0.000076); (c) the RCA territory (R=0.806; p=0.000002)

basis during PCI for ACS in 18 (17.8%) and 3 (3.0%) patients, respectively. Stenting of CA and its major branches on a third-priority basis was proposed by the computer programs and the surgeon in 66 (65.3%) and 79 (78.2%) cases, respectively (Figure 2 (b)).

Correlation analysis of priorities in the stages of the RCA territory correction proposed by the computer programs and the operating surgeon showed exact similarity in the opinions of artificial and natural intelligence in 73 cases (72.3%) (n=101; R=0.806; p=0.000002).

Computer programs regarded the RCA territory correction as the first-priority task in 40 cases (39.6%), the surgeon — in 37 cases (36.6%). It was recommended by artificial and natural intelligence to perform the RCA territory correction on a second-priority basis during PCI for ACS in 12 (11.9%) and 5 (5.0%) patients, respectively. Stenting of RCA and its major branches on a third-priority basis (at the final stage of PCI or as repeated intervention during the current hospitalization) was regarded by the computer programs and the surgeon to be appropriate in 49 (48.5%) and 57 (56.4%) cases, respectively (Figure 2 (c)).

Analyzing the survival rates in ACS patients, we noticed that 12 out of 101 patients (11.9%) with acute myocardial ischemia and three-vessel coronary artery disease died in the early postoperative period (20 days). Notably, early postoperative mortality was registered in 6 patients with STE-ACS, for whom during the intervention there was selected non-optimal sequence (as regarded by the developed programs) of repairing the three affected coronary territories (Table 2).

Discussion

Correlation analysis of priorities in the stages of correction of the LAD, CA, and RCA territories, recommended by the software and the operating surgeon, showed a lower proportion of exact similarities in the opinions of artificial intelligence and natural intelligence (57.4% for the LAD territory; 72.3% — for the CA territory; 72.3% — for the RCA territory) as compared to the results of sequence analysis proposed by the computer programs and independent experts (88.1% exact similarity for the LAD territory; 81.1% — for the CA territory; 85.1% — for the RCA territory).

The lowest proportion of exact similarities (57.4%) in computer program recommendations and opinions of the operating surgeon was found during correlation analysis of priorities in the stages of the LAD territory correction.

Correlation analysis of priorities in stages of the LAD territory correction in deceased patients (n=12), which was proposed by the computer programs and the operating surgeon, showed exact similarity in the opinions of artificial and natural intelligence in 2 out of 12 cases (16.7%) (R=0.472; p=0.120). In 10 cases (83.3%) there were differences in the sequence of

Table 2

Early postoperative mortality in STE-ACS patients (n=6)

Case	Sequence of correction recommended by computer programs and experts (1st, 2nd, 3rd priority)	Sequence of correction selected by the operating surgeon (1st, 2nd, 3rd priority)
1	1st — LAD 2nd — CA 3rd — RCA	1st — CA 2nd — LAD correction not performed 3rd — RCA correction not performed
2	1st — LAD 2nd — CA 3rd — RCA	1st — CA 2nd — LAD correction not performed 3rd — RCA correction not performed
3	1st — LAD 2nd — CA 3rd — RCA	1st — CA 2nd — LAD correction not performed 3rd — RCA correction not performed
4	1st — CA 2nd — LAD 3rd — RCA	1st — CA 2nd — LAD correction not performed 3rd — RCA correction not performed
5	1st — LAD 2nd — CA 3rd — RCA	1st — LAD 2nd — CA correction not performed 3rd — RCA correction not performed
6	1st — RCA 2nd — LAD 3rd — CA	1st — RCA 2nd — LAD correction not performed 3rd — CA correction not performed

repairing the LAD and its major branches, determined by the computer and the operating surgeon (Table 3).

Correlation analysis of priorities in stages of repairing the CA territory and its major branches (n=12), proposed by the computer programs and the operating surgeon, showed exact similarity in the opinions of artificial and natural intelligence in 4 cases (33.3%) (R=0.173; p=0.590). At the same time, in 8 cases (66.7%) there were differences in the options selected by the computer and the operating surgeon (see Table 3).

Correlation analysis of priorities in stages of repairing the RCA territory and its major branches, proposed by the computer programs and the operating surgeon, showed exact similarity in the opinions of artificial and natural intelligence in 5 out of 12 cases (41.7%) (R=0.489; p=0.106). At the same time, in 7 cases (58.3%) there were differences in recommendations (see Table 3).

The performed analysis confirms a small number of exact similarities in computer program recommendations and expert opinions concerning priorities in stages of the LAD territory correction as well as a significant number of differences (by more than 1 rank) in the opinions concerning the CA territory correction. In addition, there were quite a large number of differences in views offered by the programs and experts (by 1 rank) as to the priorities in stages of the RCA territory correction.

The results obtained reconfirm the existence of fatal mistakes in sequencing of significant three-vessel

Table 3

Similarities and differences in the sequences of correction of three coronary territories in deceased patients as recommended by the programs and the operating surgeon (absolute number/%)

Coronary territory	Exact similarity of strategies	1 rank difference in strategies	Difference in strategies higher than 1 rank
LAD (n=12; R=0.472; p=0.120)	2/16.7	3/25.0	7/58.3
CA (n=12; R=0.173; p=0.590)	4/33.3	2/16.7	6/50.0
RCA (n=12; R=0.489; p=0.106)	5/41.7	5/41.7	2/16.7

coronary disease management in ACS patients: failure to perform the intervention in the LAD territory as first priority; failure to perform the second-priority stage of coronary bed correction — adequate antegrade blood flow recovery in the CA territory — immediately after revascularization of the LAD territory; failure to perform the third-priority stage of endovascular correction of the coronary territories — adequate antegrade blood flow recovery in the RCA territory.

The data, revealed using computer programs, on the sequence of endovascular correction of three-vessel coronary disease are consistent with the findings of Sholz et al. [8], indicating that intervention in the area of clinically relevant LAD should be carried out urgently as a matter of priority in patients with ACS and three-vessel coronary disease. Besides, the viability of maximum complete myocardial revascularization in patients with ACS is proved in the studies carried out by Secemsky et al. [9] and Fukutomi et al. [10]. According to these researchers, correction of the CA and RCA territories should be performed as second and third priorities after intervention in the area of clinically relevant LAD lesion during primary percutaneous coronary intervention.

Conclusion

Appropriate time-sensitive sequencing of endovascular correction of three-vessel coronary disease is no easy and obvious task for surgeons performing endovascular interventions for acute coronary syndrome.

The developed computer programs “Sapphire 2015 — Right dominance” and “Sapphire 2015 — Left dominance” have demonstrated their efficacy when used to select the optimal sequence of three-vessel coronary disease correction in patients with acute coronary syndrome.

Recommendations for the correction of three-vessel coronary disease, obtained using the programs, reliably correlate with the expert opinion on the sequence

of repairing the left anterior descending artery, the circumflex artery, and the right coronary artery territories.

Failure to follow the optimal sequence of three-vessel coronary disease correction in patients with acute coronary syndrome leads to fatal cardiac events in the early post-percutaneous coronary intervention period.

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