Simultaneous and staged operations' immediate and long-term results in patients with the coronary and carotid arteries' combined atherosclerotic lesions

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Abstract

Objective: To study the surgical treatment's immediate and long-term results of patients with the coronary and carotid arteries' combined atherosclerotic lesions when choosing treatment tactics according to the developed a differentiated approach's algorithm. **Methods:** During the period from 01.07.2014 – 01.01.2021, 243 patients with the coronary and carotid arteries' combined atherosclerotic lesions were included in the study. Patients underwent revascularization operations on the previously developed algorithm's basis for choosing the surgical intervention's volume and stage. 104 patients (42.8%) underwent simultaneous combined coronary artery bypass grafting (CABG) and carotid endarterectomy (CEA), 139 (57.2%) patients received phased revascularization, of which 102 (73.4%) patients underwent CABG, 37 (26.6%) underwent CEA in the first stage. The endpoints both when comparing immediate and long-term results were: death from all causes, acute cerebrovascular accident (ACVA), transient ischemic attack (TIA), acute myocardial infarction (MI), as well as a combined endpoint that includes all of these events. Average follow-up time: 41.1±21.8 months. **Results:** In the early postoperative period, there weren't fatal cases in any groups. At the hospital stage, 5 (2.1%) ACVA cases, 1 (0.4%) TIA case and 3 (1.2%) acute MI cases were recorded. Long-term results were evaluated in 225 patients (92.3%). The overall survival rate was 93.8%. During the follow-up, 5 (2.4%) MI cases, 11 (4.9%) ACVA cases , 1 (1.0%) TIA case were recorded. There weren't identified significant differences between the groups stage and combined interventions for any endpoints as when comparing the immediate outcomes (acute IM p=0,680, TIA – p=0,500, ACVA – p=0,567, combined indicator, p=0,940) and remote results (mortality – 0,860, acute MI – p=0,906, TIA – p=0,528, ACVA – p=0,378, combined indicator, p=0,669). **Conclusion:** The treatment's results of patients with the coronary and brachycephalic arteries' combined atherosclerosis on the developed algorithm's basis, allows you to safely perform correction in both arterial basins and achieve satisfactory results in the hospital and long-term period.

Introduction

Coronary bypass surgery is a surgical method for the coronary heart disease's treatment. Despite its widespread use, the operation can have several complications, the most devastating of which is a postoperative stroke. The developing ACVA(acute cerebrovascular accident) 30-day risk after CABG (coronary artery bypass grafting) is 1.1% [1]. In the carotid artery damage's presence, the ACVA risk increases to 2.75%, and the 30-day mortality risk is 2.59% [2]. Coronary heart disease is the main death cause in patients with the carotid arteries' atherosclerotic lesions [3].

Patients who have undergone CEA(carotid endarterectomy) have a higher risk of developing MI(myocardial infarction) than ACVA, and patients with postoperative MI have a 5-year survival rate of only 56% [4].

To date, there aren't high-class evidence recommendations for the patients' treatment with the coronary and brachiocephalic arteries' combined atherosclerotic lesions. The ESC/ESVS Recommendations for the peripheral artery diseases' diagnosis and treatment in 2017 regarding the coronary and carotid arteries' combined atherosclerosis contain the provision: for the carotid artery revascularization in patients requiring CABG, an individual indications discussion (and if any, the method and time) is recommended for each patient by a multidisciplinary specialists' team , including a neurologist (class I, level C) [5]. ESC/EACTS recommendations on myocardial revascularization in 2018 on this issue repeat the recommendations for the patients with peripheral artery disease's management in 2017 [6]. We want to present our treating this cohort of patients' experience, to show immediate and long-term results.

Material and methods

During the period from 01.07.2014 – 01.01.2021, 243 patients with the coronary and carotid arteries' combined atherosclerotic lesions were included in the study. 104 patients (42.8%) underwent simultaneous combined CABG and CEA, 139 (57.2%) patients received step-by-step revascularization, of which 102 (73.4%) patients underwent CABG, 37 (26.6%) underwent CEA in the first stage. We determined the surgical interventions' scope and stage according to the developed by us differentiated approach algorithm. It is worth noting that the study included only patients with the planned nature of surgical interventions. Emergency patients were excluded from the study. According to the algorithm, patients with critical lesions of the carotid and coronary arteries are distinguished. A carotid arteries' critical lesion means a lesion of more than 80%. Coronary artery damage is considered critical with more than 75% stenosis. Professor Sukhanov S. G. used electromagnetic fluometry to study the relationship between the degree of the internal carotid artery lumen narrowing and volumetric blood flow. It was found that lumen stenosis up to 75% leads to a proportional decrease in blood flow. Further stenosis causes a sharp disproportionate drop in shock volume [7]. Thus, carotid artery stenosis of 80% or more was chosen by us as a critical value. It is believed that the greater the coronary artery stenosis degree, the more likely it is that the lesion is hemodynamically significant. Particular disagreements are associated with intermediate coronary lesions' revascularization (with a decrease in the vessel diameter from 50% to 70%) [8]. It is assumed that more than 70% stenosis is functionally significant. According to studies, most stenoses with angiographic severity from 50% to 70% are functionally insignificant according to the study of the blood flow fractional reserve. However, with more severe lesions (from 71% to 90%), up to 80% of all lesions cause myocardial ischemia [9]. The more than 75% coronary artery lesion was chosen by us as a critical value. The main criterion for choosing the surgical intervention tactics in patients with the coronary and carotid arteries' combined atherosclerotic lesions in our algorithm is the lesion's anatomical picture. In addition, we evaluated the clinical coronary heart disease manifestation when choosing the treatment stage. In the pain-free myocardial ischemia or stable angina presence of III–IV FC, the patient underwent CABG in the first, and CEA in the second stage. This group also included patients with FC II CHF(chronic heart failure) who had a critical isolated proximal lesion of LAD(left anterior descending) artery or in combination with other arteries. With a carotid arteries critical lesion, a coronary arteries lesion up to 75% and CHF at the level of II-III FC, the patient underwent CEA in the first, CABG in the second stage. We consider the optimal time between the surgical interventions' stages to be one month from the moment the patient is discharged after the first operation. We took into account the carotid artery lesions' "symptomality-asymptomicity" as an indication for the carotid arteries operative reconstruction according to current recommendations, however, this criterion wasn't included in the algorithm for choosing treatment tactics for combined patients. In the critical lesion presence in both arterial basins, the patient was referred for simultaneous reconstruction in the coronary and carotid arteries' basins clinical manifestations regardless. In this way, we prevent vascular events that may occur in the perioperative period after intervention on one arterial bed due to a critical hemodynamic disorder in the non-operated pool.

This algorithm is adopted in the Federal Center for Cardiovascular Surgery named after S. G. Sukhanov to determine the treatment tactics in patients with multifocal atherosclerosis. The study design was developed to confirm its hypothesis' validity (Figure 1).

We analyzed the preoperative clinical indicators of patients in each groups. There wasn't significant difference in the any characteristics (Table I).

Angiographic studies

The angiographic studies characteristics of coronary and BCA are shown in Table II. In a statistical study, a significant intergroup difference in coronary and carotid artery lesions was obtained. This fact is explained by the fact that patients were divided into groups primarily according to the lesion angiographic picture. Depending on this, the surgical treatment tactics and scope were determined.

The primary endpoints were death from all causes, ACVA, TIA(transient ischemic attack), acute MI, as well as a combined endpoint including death from all causes, acute MI, ACVA and TIA. The assessment was carried out at the hospital stage and in the long-term postoperative period.

Quantitative traits comparison in the groups was carried out using the Mann–Whitney and Kraskell-Wallis criteria. Pearson's chi-squared test was used to evaluate qualitative features. The research results were processed using the Statistica for Windows 13 application software package (Statsoftlnc., USA). The survival function was calculated using the Kaplan-Mayer method. The results are presented in the form Kaplan-Meyer curves graphs indicating the logrank test significance level to determine the difference in the studied groups. The risk period for the event occurrence was determined in months for each patient. Each period between the inclusion moment in the study and the event occurrence or the end of the study represented a separate observation.

Immediate results (during hospitalization)

There weren't fatal cases registered during hospitalization. In total, 6 (2.5%) neurological complications' cases and 3 (1.2%) acute MI cases were registered: in the simultaneous interventions' group, 3 (2.9%) ACVA and 1 (0.9%) MI, in the group with the first stage of CABG - 2 (2.0%) ACVA, 1 (1.0%) TIA and 1 (1.0%) MI, in the group with the first stage of CEA - 1 (2.7%) ACVA. The groups had similar combined results - 4 (3.9%) for the group with the first stage of CABG, 1 (2.7%) for the group with the first stage of CEA and 4 (3.8%) for the combined group. There wasn't significant difference in any endpoints (Table III).

All ACVA cases occurred by the time the patient woke up after surgery. In the combined interventions' group, in one case ACVA appeared in the middle cerebral artery basin from the operated side. Given the reconstruction zone patency according to MSCT AG BCA(brachiocephalic arteries), the complication is probably associated with ischemia during the carotid arteries compression. The second and third ACVA cases manifested themselves in the posterior cerebral artery basin. Acute antero-lateral MI in the combined group was recorded on the fourth day after mammarocoronary bypass surgery and CEA on the right in a patient with right coronary artery chronic occlusion and diffuse critical lesion of the envelope artery throughout. Angiography was performed – mammary graft is passable.

In the stage-by-stage interventions' group, both ACVA cases in the affected carotid artery basin were recorded in the early postoperative period in patients who underwent CABG at the first stage. One patient had TIA in the affected carotid artery pool on the third day after CABG. All patients underwent CEA on average one month after the first stage. One patient had a acute MI clinic along the anterior-lateral wall on the second day after the first stage of the CEA. According to emergency indications, CABG was performed. In the staged interventions' group with the first stage of CABG, in one case, ischemia along the anterior wall occurred on the first day after surgery. According to the angiography, an occlusion of the mammary graft was revealed. Given the anterior descending artery diffuse lesion to the periphery, there are high risks of repeated revascularization - acute MI was conservatively conducted.

Long-term results

Telephone or clinical interviews were conducted in April 2021. For staged operations' groups, the assessment was carried out after both stages of reconstructive interventions were performed. The maximum follow–up time for the patient was 78 months, the minimum was 4 months. Average follow-up time: 41.1±21.8 months. The endpoints were death from all causes, ACVA, TIA, MI, as well as a combined endpoint, including death from all causes, acute MI, ACVA, TIA during the patient's hospitalization.

We managed to contact 225 patients out of 243 operated (92.6%). We were unable to find out long-term results in 3 patients from the staged interventions' group (the first stage of CABG), 7 patients from the staged interventions' group (the first stage of CEA) and 8 patients from the combined interventions' group. The overall survival rate was 93.8% (92.9% for the stage group (the first stage of CABG), 93.3% for the stage group (the first stage of CEA) and 94.8% for the combined interventions' group, p=0.807). 14 people died (6,2%) – 7 (7,1%) in the group with the first stage of CABG, 2 (6.7%) in the group with the first stage of CEA and 5 (5.2%) in the combined group. In total, 5 (2.4%) MI cases – 2 (9.1%) were recorded in the group with first performed CABG, 1 (3.3%) in the group with first performed CEA and 2 (2.1%) in the combined group, and 11 (4.9%) ACVA cases – 4 (4.0%) in the group with first performed CABG, 3 (10%) in the group with first performed CEA and 4 (4.1%) in the simultaneous interventions' group. There was also 1 (1.0%) TIA case in the stage group (the first stage of CABG). One person in the combined group died from MI, there weren't fatal cases from MI in the staged interventions' group. 1 person died from ACVA in both stage groups and 1 person in the combined group. The combined point was 15 (15.2%) in the stage group (the first stage of CABG), 5 (16.7%) in the stage group (the first stage of CEA) and 11 (10.6%) in the combined group. There weren't identified significant differences between groups in the any studied parameters and endpoints (Table. IV).

In the analysis by Kaplan-Meier survival within 6 years in the simultaneous interventions' group represented 94.8% in the group stage of the interventions (first stage CABG) – 92,9% in the group stage of the interventions (the first stage of the CEA) – 93,3% with corresponding 95% confidence intervals (Figure 2A). In the survival analysis by logrank test isn't statistically significant differences ($\chi2$=0,487, p=0,784).

The groups didn't differ in terms of freedom from MI in the long-term postoperative period (Figure 2B). For the combined group, this indicator was 97.9%, for the stage group (the first stage of CABG) – 97.9%, for the group of stage interventions (the first stage of CEA) – 96.7% ($\chi2$=0.013, p=0.994).

When analyzing the freedom from ACVA according to the logrank criterion, there also weren't differences between the groups (Figure 2C). Thus, the indicator for the combined group was 95.8%, for the stage group (the first stage of CABG) – 95.7%, for the stage group (the first stage of CEA) - 90.0% ($\chi2$=0.410, p=0.815).

When comparing the freedom from the combined endpoint complications (mortality from all causes + MI+ACVA+TIA) by the Kaplan-Mayer method, several events summation in one patient didn't occur, but it was believed that one complication occurred, due to this method's peculiarities. Freedom from the combined indicator development (lethality from all causes + MI+ACVA+TIA) for 6 years was 91.7% for the simultaneous interventions' group, 87.9% for the group in which CABG was performed at the first stage and 86.7% for the group in which the first stage was performed CEA ($\chi2$=0.952, p=0.621) (Figure 2D).

Discussion

There isn't still consensus not only on the treatment, but also on the diagnosis and detection of arterial basins concomitant asymptomatic lesions. In 2015, the randomized trial results proving the need for CAG before CEA were published. 426 patients in need of CEE were randomized into two groups. 30-day results in the group who received CAG showed no acute MI cases and zero mortality. At the same time, in the group without coronary angiography, the 30-day acute MI frequency was 4.3%, and the mortality rate was 0.5%. In the long-term 6-year study results in CAG, the acute MI incidence was 1.4%, in the group without CAG – 15.7%, and the mortality rate was 0 (0%) and 2.9%, respectively [10].

We analyzed patients who underwent the coronary and carotid arteries revascularization from 1.07.2014 to 01.01.2021 at the Federal Center for Cardiovascular Surgery named after S. G. Sukhanov. Of the 7,716 patients who underwent CABG, 1,597 (20.7%) patients had BCA lesion. Moreover, 430 (5.6%) of them underwent the carotid arteries revascularization. At the same time, out of 681 patients who received CEA and CAS(carotid arteries stenting), 430 (63.1%) patients underwent CABG. Such a occurrence high rate of severe coronary atherosclerosis in patients going for the carotid arteries revascularization can be explained by the fact that in the Federal Center for Cardiovascular Surgery named after S. G. Sukhanov's patients are mostly referred for coronary angiography and the coronary arteries' revascularization, and carotid artery damage is detected during follow-up examination. Despite this amendment, such a combined atherosclerosis frequent occurrence allows us to conclude that a screening ultrasound study of the brachiocephalic arteries before coronary revascularization and coronary angiography before intervention on the carotid arteries is necessary.

The mechanisms underlying the increased stroke risk in CABG are multifactorial. We shouldn't forget that carotid artery atherosclerosis isn't the only ischemic stroke predictor in CABG. Aortic atheromatosis is probably an even more significant factor. Most CABG operations are performed using artificial circulation with cannulation and aortic compression; even if they are performed without ABC, the aorta is often manipulated to create proximal anastomoses. According to our research, the epiaortic scanning use reduces mortality by 5 times, and the stroke risk is reduced by 12 times [11]. It is necessary to perform an epiaortic scan on a routine basis at each operation, even without ABC. When detecting aortic atheromatosis, the surgeon must have the full revascularization range techniques and choose the appropriate one. It is important to remember about the hybrid revascularization possibility to minimize manipulations on the aorta with severe atheromatosis. In our study, operations were performed both with and without ABC, and when detecting the aorta atheromatosis, the changing the place of cannulation methods, "single clamp", "no touch aorta" and hybrid revascularization were used. We assume that routine epiaortic scanning is one of the factors for obtaining satisfactory results at the hospital stage.

To prevent intraoperative brain desaturation associated with ischemic complications, continuous monitoring using near-infrared spectroscopy is recommended [12]. Neuromonitoring allows to change the surgery strategy with a significant drop in cerebral saturation and reduce the carotid arteries compression time, thereby preventing ischemic damage. But stable brain oximetry indicators are also important. Most surgeons try to minimize the carotid arteries compression time, thereby reducing the ischemia time. Sometimes this can lead to incomplete endarterectomy with fixed plaque particles remnants in the lumen. Stable neuromonitoring indicators allow the surgeon to work calmly without undue haste and perform endarterectomy as fully as possible with the all fixed and floating plaque particles removal without ischemic damage fear due to long carotid arteries compression. The cerebral damage mechanism after cardiac surgery with the artificial circulation use hasn't yet been fully studied. Pathogenesis may include embolization or hypoperfusion causing cerebral ischemia. Cerebral oximetry monitoring is necessary when performing CABG in patients with combined carotid artery disease. This makes it possible to prevent ischemia both in ABC and when performing surgery without artificial circulation, in which the heart is positioned with hypotension periods. In this study, we used cerebral oximetry in all operations.

To date, there are a significant strategies number and algorithms for choosing treatment tactics for patients with the coronary and carotid arteries combined atherosclerotic lesions. In 2020, the results of a major meta-analysis were published. This meta-analysis included eleven studies with a total of 44,895 patients (21,710 in the combined group and 23,185 patients in the phased group). In the simultaneous CEA and CABG group, there was a statistically significantly lower MI risk and a higher stroke and death risk. The TIA frequency, postoperative bleeding, and pulmonary complications were the same between the two groups [13]. According to the our study results, the complications risks in staged and combined operations with a differentiated approach to the treatment tactics choice are comparable.

Conclusions

The tactics choice for the treatment of the coronary and carotid arteries combined atherosclerotic lesions has been a problem for clinicians for four decades. In the absence of randomized controlled trials, recommendations for these patients management are based on the single-center retrospective studies results. The surgical treatment options multitude for both conditions makes it difficult to reach a clear consensus on the optimal one. In our opinion, the lesion angiographic picture in planned patients, together with the clinical picture, should play a key role in choosing the surgical treatment tactics. In a critical lesion case in both arterial basins, performing simultaneous reconstruction allows preventing vascular events that may occur with the staged interventions' nature. The complications risks with the coronary and carotid arteries simultaneous revascularization in a more severe patients cohort, as well as long-term survival and freedom from vascular events, don't differ in comparison with patients who received staged interventions in the coronary and carotid basins.

References

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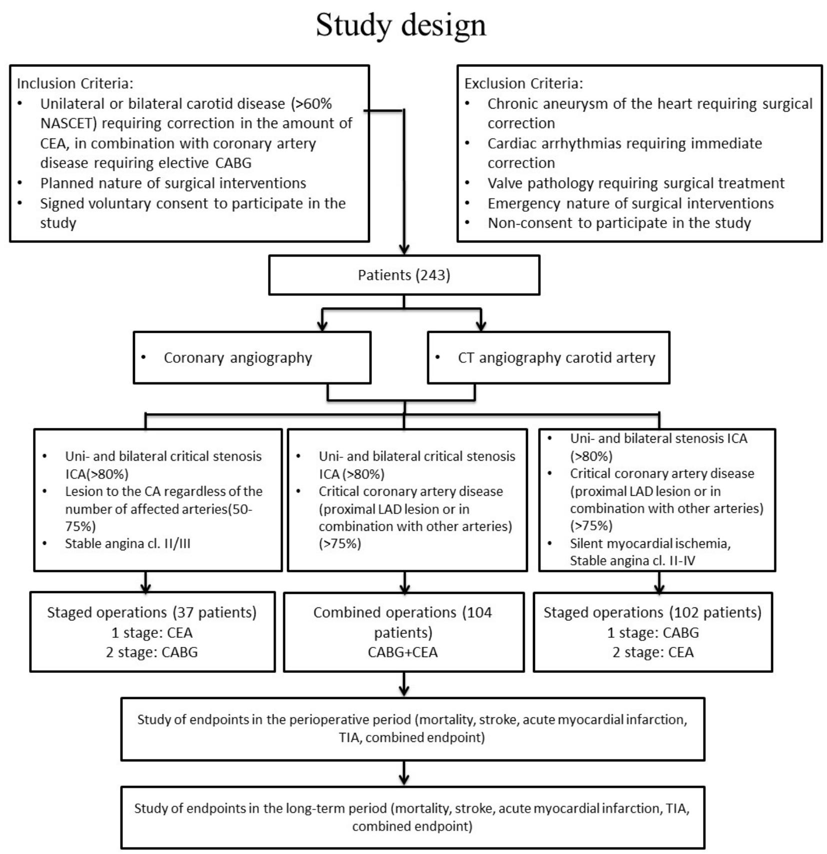
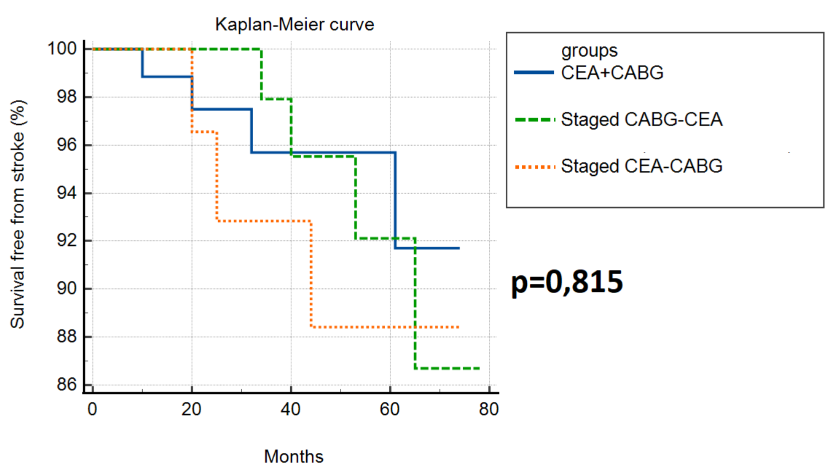

Study design
Inclusion Criteria:
• Unilateral or bilateral carotid disease (>60% NASCET) requiring correction in the amount of CEA, in combination with coronary artery disease requiring elective CABG
• Planned nature of surgical interventions
• Signed voluntary consent to participate in the study
Exclusion Criteria:
• Chronic aneurysm of the heart requiring surgical correction
• Cardiac arrhythmias requiring immediate correction
• Valve pathology requiring surgical treatment
• Emergency nature of surgical interventions
• Non-consent to participate in the study
Patients (243)
• Coronary angiography
• CT angiography carotid artery
• Uni- and bilateral critical stenosis ICA(>80%) • Lesion to the CA regardless of the number of affected arteries(50-75%) • Stable angina cl. II/III
• Uni- and bilateral critical stenosis ICA (>80%) • Critical coronary artery disease (proximal LAD lesion or in combination with other arteries) (>75%)
• Uni- and bilateral stenosis ICA (>80%) • Critical coronary artery disease (proximal LAD lesion or in combination with other arteries) (>75%) • Silent myocardial ischemia, Stable angina cl. II-IV
Staged operations (37 patients) 1 stage: CEA 2 stage: CABG
Combined operations (104 patients) CABG+CEA
Staged operations (102 patients) 1 stage: CABG 2 stage: CEA
Study of endpoints in the perioperative period (mortality, stroke, acute myocardial infarction, TIA, combined endpoint)
Study of endpoints in the long-term period (mortality, stroke, acute myocardial infarction, TIA, combined endpoint)


Kaplan-Meier curve
Survival free from stroke (%)
100
98
96
94
92
90
88
86
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60
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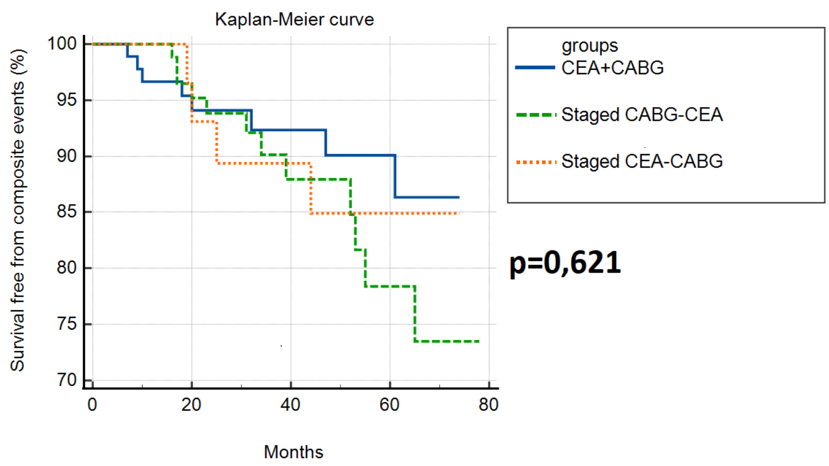
Months
groups
CEA+CABG
Staged CABG-CEA
Staged CEA-CABG
p=0,815


Kaplan-Meier curve
Survival free from composite events (%)
100
95
90
85
80
75
70
0
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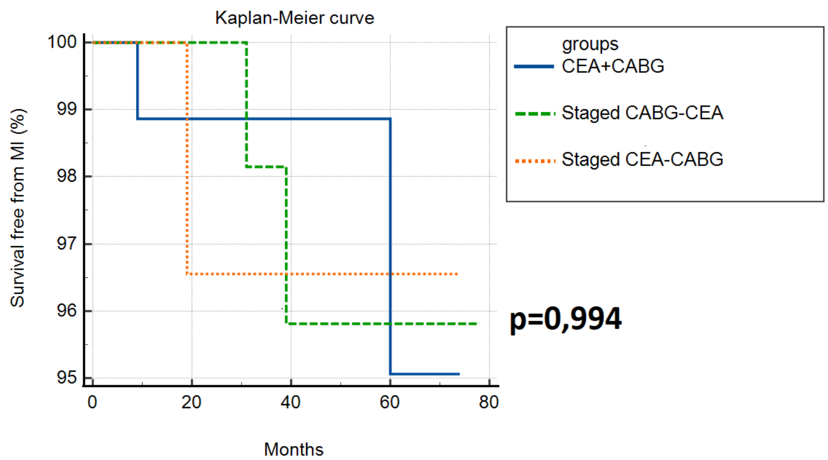
Months
groups
CEA+CABG
Staged CABG-CEA
Staged CEA-CABG
p=0,621


Kaplan-Meier curve
Survival free from MI (%)
100
99
98
97
96
95
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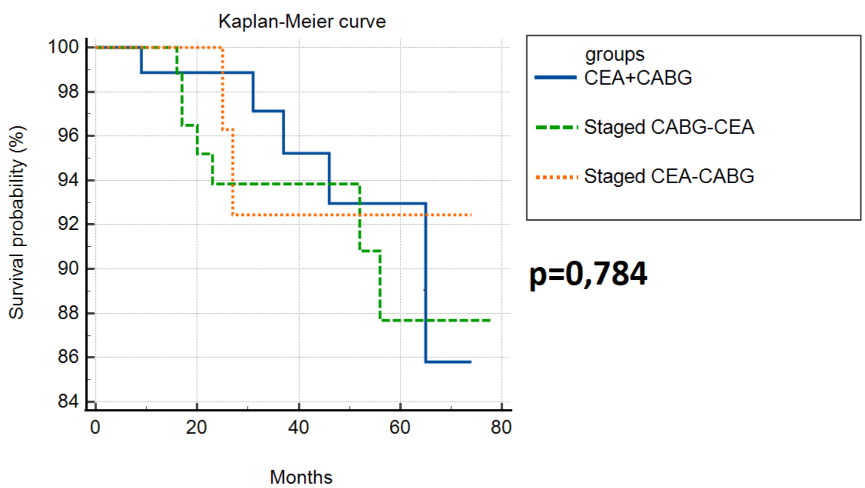
Months
groups
CEA+CABG
Staged CABG-CEA
Staged CEA-CABG
p=0,994


Kaplan-Meier curve
Survival probability (%)
100
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92
90
88
86
84
0
20
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60
80
Months
groups
CEA+CABG
Staged CABG-CEA
Staged CEA-CABG
p=0,784

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