SURVIVAL RATE IN MULTIFOCAL ATHEROSCLEROSIS PATIENTS WHO UNDERWENT SURGICAL CAROTID AND CORONARY TERRITORIES REVASCULARISATION

[2]Grygoruk S., [1,2]Sirko A., [1,2]Dudukina S., [3]Matsuga O.

[1]State Establishment, Dnipropetrovsk Medical Academy, Ministry of Healthcare of Ukraine;
[2]Public Institution, Mechnikov Dnipropetrovsk Regional Clinical Hospital, Dnipro;
[3]Oles Honchar Dnipro National University, Ukraine

In patients with combined atherosclerotic lesions of coronary and cerebral arteries, the risk of stroke after cardiac surgeries increases significantly. Consequently, the risk of a heart attack during main head and neck artery surgery also increases [1,7]. Given this risk, it would be useful to determine the sequence of surgeries and their timings and identify short- and long-term treatment outcomes. To date, the short-term outcomes of cerebral and coronary artery revascularisation surgeries performed with different methods and different timings have been well studied [6,9,4], but the long-term outcomes have not.

The study aim was to determine the long-term survival rates in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent surgical revascularisation of both territories.

Material and methods. This was a prospective study of survival rates in 329 patients with multifocal atherosclerosis who underwent surgical revascularisation of carotid and coronary territories. All carotid territory revascularisation surgeries and endovascular coronary territory revascularisation surgeries were performed in Mechnikov Dnipropetrovsk Regional Clinical Hospital. Open cardiac surgeries were performed in the Dnipropetrovsk Regional Cardiology and Cardiac Surgery Center. The study included patients of both sexes with atherosclerotic lesions of the carotid and coronary territories requiring surgical intervention. The exclusion criteria were express heart rhythm or conduction disorder, concomitant incurable pathology and patient refusal to participate in the study.

Concomitant pathology manifested itself as acute ischaemic cerebrovascular disturbances in 60.7% of the patients (ischaemic stroke or transitory ischaemic attack). A concomitant pathology was revealed during the follow-up examination. In patients whose disease onset was associated with cardiac pathology, diagnosis of atherosclerotic carotid artery lesion was performed within comprehensive atherosclerotic patient examinations using transcranial Doppler on a 77025A Hewlett Packard Ultrasound System, 1996. All participants underwent cerebral and coronary angiography using a Philips-Integris V-3000 Angiography System with Ultravist-370 (Schering, Germany) and Omnipaque (Huffslung Nycomed, Austria). Brain computed tomography was performed by using an H1S CT/e Dual E7CS04037 GE Computed Tomography Scanner (General Electric).

Depending on the technique and timing of surgical revascularisation for a particular territory, the patients were divided into six clinical study groups. The first group included 75 patients who underwent carotid endarterectomy (CEA) followed by (after different intervals) coronary artery bypass grafting (CABG). The second group included 31 patients who underwent cerebral artery stenting (CERAS) followed by CABG during the same hospitalisation. The third group included 28 patients who underwent CERAS followed by (after different intervals) coronary arteries stenting (CORAS). In the fourth group, 61 patients underwent CORAS prior to CEA. The fifth group included 50 patients who underwent simultaneous cerebral and coronary artery stenting (CERAS + CORAS). In the sixth group, 36 patients underwent CEA followed by simultaneous CEA + CABG surgery.

Indications for surgical carotid arteries and cardiac vessel intervention were determined by a neurosurgeon and cardiac surgeon, respectively, whereas indications for simultaneous surgeries were assessed in a specialty surgeons conference. For CEA, a conventional method was used, whereas all CABG surgeries were performed with cardiopulmonary bypass.

In each group, a survival function was analysed starting from Day 30 postoperatively using the Kaplan–Meier estimator. Data were collected by administering a written questionnaire to determine a patient's post-treatment quality of life, whereas the date of a patient's death was provided (or reported via phone surveys) by relatives.

The Kaplan–Meyer estimator of survival function at time point *t* was calculated according to the following formula [5]:

$$\hat{S}(t) = \prod_{i:t_i \le t} \left(1 - \frac{d_i}{n_i}\right),$$

where t_i = time point when at least one patient died;

d_i = number of patients who died at time point t_i;

n_i = number of patients who survived up to time point t_i, excluding the deceased.

The confidence interval of survival at time point *t* with a confidence probability of 1 – a was determined according to the following formula [5]:

$$\exp\left(-\exp\left(c_+(t)\right)\right) < S(t) < \exp\left(-\exp\left(c_-(t)\right)\right)$$

where

$$c_\pm(t) = \ln\left(-\ln \hat{S}(t)\right) \pm z_{1-\alpha/2}\sqrt{\hat{V}};$$

$$\hat{V} = \frac{1}{\left(\ln \hat{S}(t)\right)^2} \sum_{i:t_i \le t} \frac{d_i}{n_i\left(n_i - d_i\right)};$$

$z_{1-\alpha/2}$ = quantile of standard normal distribution.

For the purposes herein, a 95% confidence interval was used; i. e., a = 0.05.

The survival functions in different groups were compared by using the log-rank test [5]. The main hypothesis was that survival rates in the groups were similar and that differences were random; that is, survival function variation is indistinguishable. Such criterion was based on the following statistic:

$$z = \frac{\sum_{i:t_i \le t} \left(d_{1,i} - E_{1,i}\right)}{\sqrt{\sum_{i:t_i \le t} V_{1,i}}},$$

where $d_{1,i}$, $d_{2,i}$ = number of patients in groups 1 and 2, respectively, who died at time point t_i;

$n_{1,i}$, $n_{2,i}$ = number of patients in groups 1 and 2, respectively, who survived up to time point t_i;

$d_i = d_{1,i} + d_{2,i}$; $n_i = n_{1,i} + n_{2,i}$;

$$E_{1,i} = d_i \frac{n_{1,i}}{n_i}; \quad V_{1,i} = \frac{d_i n_{1,i} n_{2,i} \left(n_i - d_i\right)}{n_i^2 \left(n_i - 1\right)}.$$

Statistical distribution of z converges to standard normal one. Therefore, the *p*-value was calculated according to the following formula:

$$p = 2\left(1 - \Phi\left(|z|\right)\right),$$

where $\Phi(\square)$ = standard normal distribution.

If p ³ a, there are no reasons to reject the main hypothesis and the survival function in the groups can be considered indistinguishable. For the purposes herein, a = 0.05 was used. The survival functions in the groups were evaluated and compared by using Jupyter Notebook and the lifelines library for Python.

Results and their discussion. Early postoperative mortality rates were as follows: 4% in the first group, 2.5% in the second group, 3.4% in the third group, 1.7% in the fourth group, 3.9% in the fifth group and 2.9% in the sixth group. In the first group, which included patients who underwent CEA at various time periods prior to CABG, the 10-year survival after myocardial revascularisation was 46% [CI 95%, 58%–34%] (Fig. 1). The figure also shows that in the first 3 years, 25% of first group patients died (survival function is 75% [CI 95%, 83%–63%]). A decreased survival function was more significant during the first 5 years of follow-up, whereas the function graph was almost flat from 5 to 10 years after the surgery (the 5-year survival rate was 60% [CI 95%, 71%–48%].

In the second group, which included the patients who underwent CERAS immediately before CABG, the 10-year survival rate after the surgery was only 19% [CI 95%, 34%–7%] (Fig. 2). A function decrease was observed evenly throughout the follow-up period (3-year survival rate, 83% [CI 95%, 92%–67%]; 5-year survival rate, 56% [CI 95%, 70%–39%]).

The third group of patients who underwent CERAS followed by CORAS after different intervals had sharply decreased survival functions at 5 years (69% [CI 95%, 83%–48%]) and 7 years (42% [CI 95%, 60%–23%] years after the surgery) (Fig. 3). The 10-year survival rate was 27% [CI 95%, 46%–10%]. In the fourth group, which included the patients who underwent CORAS prior to CEA to prevent cardiac complications (Fig. 4), the 10-year survival rate was 49% [CI 95%, 62%–34%]. The first significant decrease in the 10-year survival rates was registered at year 5 of follow-up (the 5-year survival rate was 86% [CI 95%, 93%–72%]) and then it gradually and uniformly decreased to the indicated values.

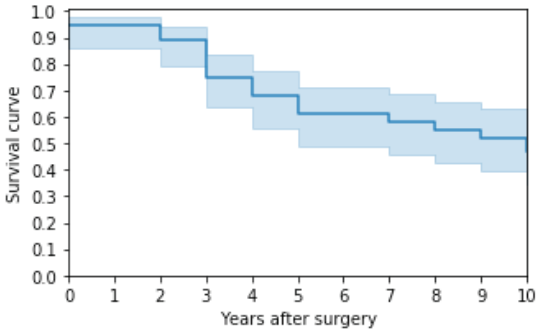

Fig. 1. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent CEA at various time periods prior to CABG

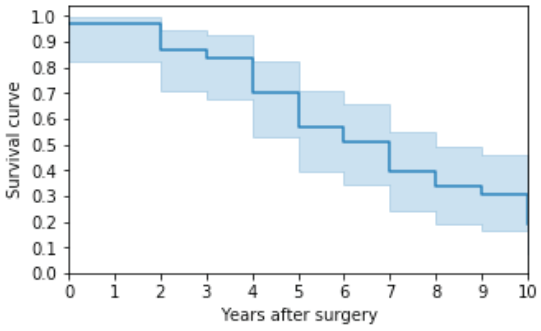

Fig. 2. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent CERAS prior to CABG

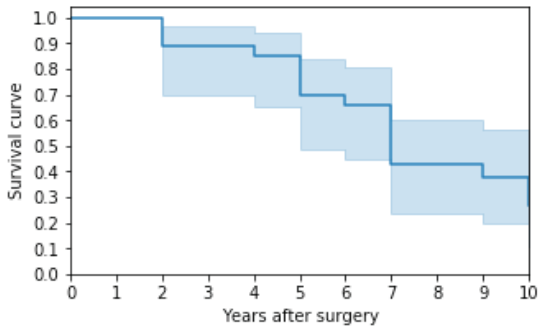

Fig. 3. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who subsequently underwent CERAS and CORAS

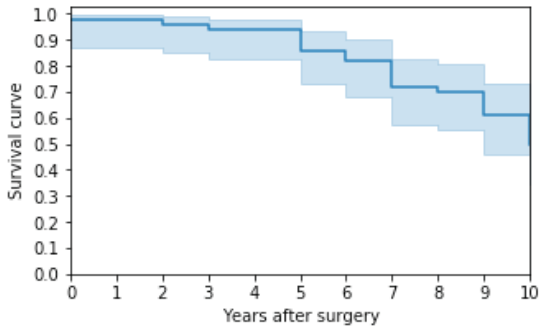

Fig. 4. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent CORAS prior to CEA

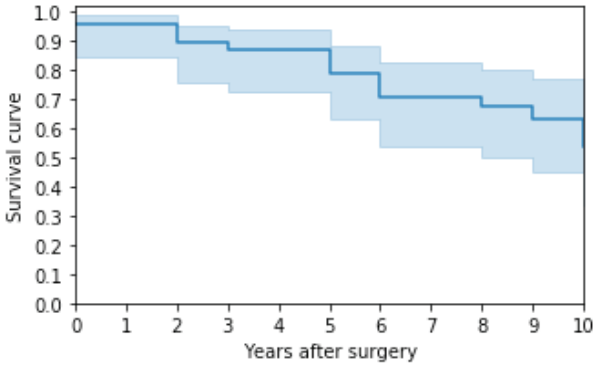

Fig. 5. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent simultaneous CERAS and CORAS

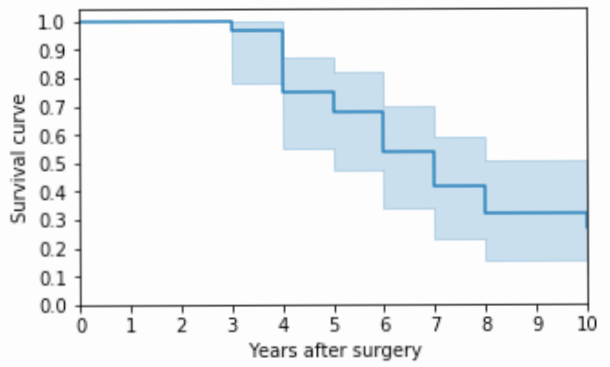

Fig. 6. Survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent simultaneous CEA + CABG

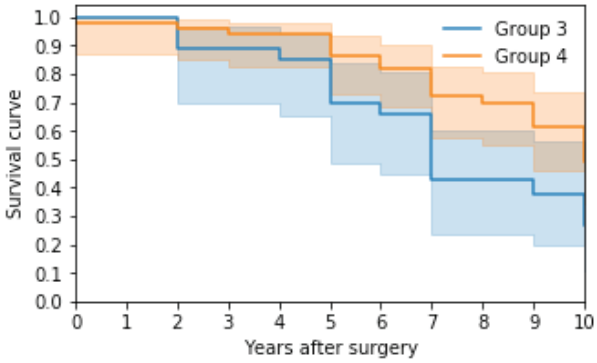

Fig. 7. Comparison of 10-year survival rate functions between CERAS performed prior to CABG and for simultaneous CEA + CABG

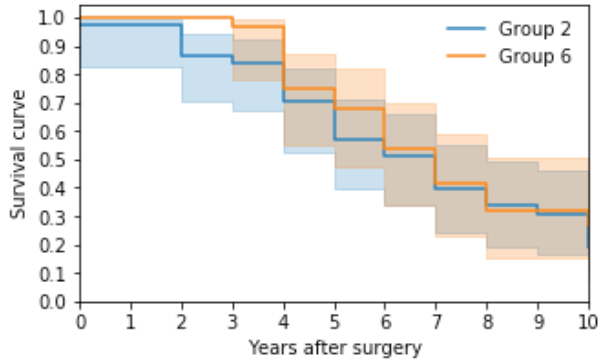

Fig. 8. Comparison of 10-year survival rate functions between endovascular revascularisation of both territories (CERAS + CORAS) and combined surgery (CORAS + CEA)

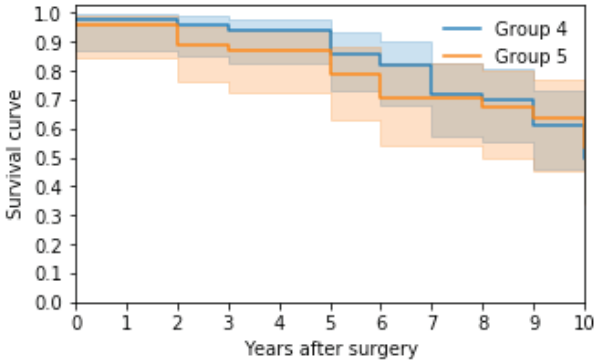

Fig. 9. Comparison of 10-year survival rate functions between CORAS prior to CEA and simultaneous CORAS + CERAS

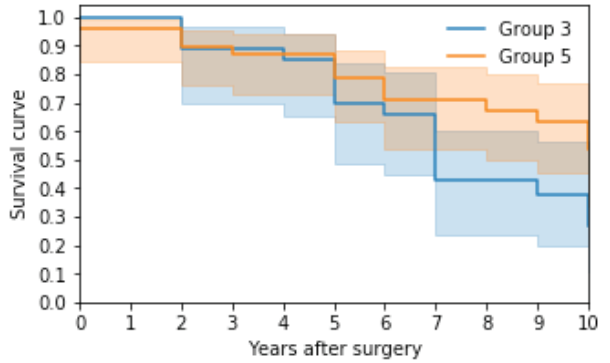

Fig. 10. Comparison of 10-year survival rate functions between endovascular surgery with sequential and simultaneous CERAS + CORAS

In the fifth group, which included patients who underwent simultaneous CERAS and CORAS, the 3-year survival rate was 86% [CI 95%, 93%–72%], the 5-year survival rate was 78% [CI 95%, 88%–63%] and the 10-year survival rate was 53% [CI 95%, 69%–33%]. The survival function decreased uniformly (Fig. 5). In the sixth group, which included the patients who underwent simultaneous CEA + CABG, the survival function plateaued during the first 3 years after the surgery (Fig. 6). Its sharp decrease was registered in year 4 of the follow-up. The 5-year survival rate was 67% [CI 95%, 81%–47%]. Then, the survival function decreased gradually and significantly, with a 7-year survival rate of 41% [CI 95%, 58%–22%] and a 10-year survival rate of 26% [CI 95%, 45%–11%].

The main causes of death in all groups were cardiac and cerebral events. Several patients died from other causes. A comparison of survival functions was performed for the groups in which alternative methods of carotid and coronary territory revascularisation were applied.

Figure 7 shows that the 10-year survival rates in patients did not significantly differ between CERAS performed prior to CABG and simultaneous CEA + CABG (p=0.532).

During the first 5 years after carotid and coronary territory revascularisation, the survival functions were similar between patients who underwent endovascular revascularisation of both territories (CERAS+CORAS) and those who underwent com-

bined surgery (CORAS+CEA); the 5–10-year postoperative survival rates were higher in patients who underwent combined surgery (p=0.026) (Fig. 8).

The survival functions in patients who underwent simultaneous CERAS + CORAS and CORAS prior to CEA did not differ significantly (p=0.93). Nevertheless, Fig. 9 shows that after the surgery, the 2–7-year survival rates were somewhat higher in the fourth group.

After endovascular revascularisation of both territories (sequentially or simultaneously), there was no significant difference in the 10-year survival rates (p=0.07). Nevertheless, Fig. 10 shows that starting from year 7 of the follow-up, the survival rate in patients who underwent simultaneous cerebral and coronary arteries stenting was somewhat higher.

The main limitation of this study was that individual differences in the survival function of combined atherosclerotic cerebral and coronary artery lesions among the groups were underestimated.

In recent years, the survival rate for multifocal atherosclerosis patients who underwent surgical carotid and coronary territory revascularisation has significantly improved because of the development of endovascular technologies and improved techniques of open cardiac and carotid artery surgeries. Along with improved surgical techniques, the possibility of improved time management, such as when performing simultaneous surgeries for combined atherosclerotic lesions of several territories (in particular, carotid and coronary territories), has been studied [9, 4]. According to different authors, the survival rate after simultaneous CEA + CABG surgery depends on age, concomitant diseases, risk factors and preoperative condition. The survival rates for years 1, 3 and 5 after simultaneous CEA + CABG were 90%, 82% and 73%, respectively [3,8]. The 3-year survival rate of patients who underwent SCA + CABG has previously been found to be 81% [2]. Our study determined the survival functions for patients who underwent carotid and coronary territory revascularisation surgeries using different methods. The results of the 5-year survival functions were not significantly different from the results obtained from similar studies.

The 10-year survival rate in patients with combined atherosclerotic cerebral and coronary artery lesions has not been extensively reported in modern literature. The data from our study showed no statistically significant differences in the 10-year survival rates between patients who underwent simultaneous CEA + CABG surgeries (26%) and combined surgeries (CERAS + CABG) (19%) and showed higher survival rates in the patients who underwent combined surgeries (CORAS+ CEA) relative to those who underwent CERAS + CEA surgeries.

The results of this study can be useful for selecting the tactics of surgical cerebral and coronary artery revascularisation, identifying the sequence of respective surgeries and time management.

Prospects for further research. Increased postoperative survival rates, particularly after carotid and coronary territories revascularisation, are associated with advances in medical technologies and the pharmacological industry. However, the long-term quality of life in respective patient populations after revascularisation of the two most important vascular territories has been poorly studied previously. There are opportunities for future research on patients' quality of life, including their cognitive functions and if necessary, development of methods that might correct any deficits.

REFERENCES

1. Cheng H, Udesh R, Mehta A, Thirumala PD. Perioperative strokes after coronary artery bypass grafting with staged carotid endarterectomy: A nationwide perspective. // J Clin Anesth. 2017 Jun;39:25-30.
2. Chiariello L, Nardi P, Pellegrino A, Saitto G, Chiariello GA, Russo M, Zeitani J, Versaci F. Simultaneous carotid artery stenting and heart surgery: expanded experience of hybrid surgical procedures. // Ann Thorac Surg. 2015 Apr;99(4):1291-7.
3. Chiti E1, Troisi N, Marek J, Dorigo W, Innocenti AA, Pulli R, Stefano P, Pratesi C. Combined carotid and cardiac surgery: improving the results. //Ann Vasc Surg. 2010 Aug;24(6):794-800.
4. Feldman DN, Swaminathan RV, Geleris JD, Okin P, Minutello RM, Krishnan U, et.al. Comparison of Trends and In-Hospital Outcomes of Concurrent Carotid Artery Revascularisation and Coronary Artery Bypass Graft Surgery: The United States Experience 2004 to 2012. // JACC Cardiovasc Interv. 2017 Feb 13;10(3):286-298.
5. Hosmer D., Lemeshow S., May S. Applied Survival Analysis: Regression Modeling of Time-to-Event Data. 2nd ed. New York: John Wiley & Sons, 1999. 416 p.
6. Paraskevas KI, Nduwayo S, Saratzis AN, Naylor AR. Carotid Stenting Prior to Coronary Bypass Surgery: An Updated Systematic Review and Meta-Analysis. // Eur J Vasc Endovasc Surg. 2017 Mar;53(3):309-319.
7. Pinto Sousa P, Teixeira G, Gonçalves J, Veiga C, Sá Pinto P, Brandão P, Canedo A, Vouga L, Almeida R. Carotid Stenosis in Cardiac Surgery Patients. // Rev Port Cir Cardiotorac Vasc. 2017 Jul-Dec;24(3-4):126.
8. Ren S1, Liu P, Ma G, Wang F, Qian S, Fan X. Long-term outcomes of synchronous carotid endarterectomy and coronary artery bypass grafting versus solely carotid endarterectomy. // Ann Thorac Cardiovasc Surg. 2012;18(3):228-35.
9. Zhang J, Xu RW, Fan X, Ye Z, Liu P A Systematic Review of Early Results Following Synchronous or Staged Carotid Artery Stenting and Coronary Artery Bypass Grafting. // Thorac Cardiovasc Surg. 2017 Jun;65(4):302-310.

SUMMARY

SURVIVAL RATE IN MULTIFOCAL ATHEROSCLEROSIS PATIENTS WHO UNDERWENT SURGICAL CAROTID AND CORONARY TERRITORIES REVASCULARISATION

[2]Grygoruk S., [1,2]Sirko A., [1,2]Dudukina S., [3]Matsuga O.

[1]State Establishment, Dnipropetrovsk Medical Academy, Ministry of Healthcare of Ukraine; [2]Public Institution, Mechnikov Dnipropetrovsk Regional Clinical Hospital, Dnipro; [3]Oles Honchar Dnipro National University, Ukraine

Aim - short-term outcomes of cerebral and coronary artery revascularisation surgeries performed with different methods and different timing have been well studied, but the long-term outcomes have not.

The study aim was to determine the long-term survival rates in patients with combined atherosclerotic cerebral and coronary artery lesions who underwent surgical revascularisation of both territories.

We evaluated the survival functions of six groups of patients with combined atherosclerotic cerebral and coronary artery le-

sions who underwent revascularisation using different methods in different sequences and at different time periods of both territories. Survival in each group was determined from postoperative Day 30 by using the Kaplan–Meier method and compared by using the log-rank test. Survival was also compared among the groups in which alternative methods of carotid and coronary territories revascularisation were used.

The 5-year survival rates were similar between patients who underwent endovascular revascularisation of both territories (cerebral and coronary arteries stenting) or combined surgery (coronary arteries stenting + carotid endarterectomy). The 5–10-year survival rate was higher in patients who underwent combined surgery than in the other patients (p=0.026). The main causes of death in all groups were cardiac or cerebral events. The 10-year survival rates did not significantly differ between patients who underwent cerebral artery stenting prior to coronary artery bypass grafting and those who underwent simultaneous carotid endarterectomy + coronary artery bypass grafting (p=0.532).

The results of this study can be useful for selecting the tactics of surgical cerebral and coronary artery revascularisation, identifying the sequence of respective surgeries and time management.

Keywords: carotid and coronary arteries atherosclerosis, cerebral and coronary arteries stenting, carotid endarterectomy.

РЕЗЮМЕ

ВЫЖИВАЕМОСТЬ БОЛЬНЫХ МУЛЬТИФОКАЛЬНЫМ АТЕРОСКЛЕРОЗОМ, ПЕРЕНЕСШИХ ХИРУРГИЧЕСКУЮ РЕВАСКУЛЯРИЗАЦИЮ КАРОТИДНОГО И КОРОНАРНОГО БАССЕЙНОВ

[2]Григорук С.П., [1,2]Сирко А.Г., [1,2]Дудукина С.А., [3]Мацуга О.Н.

[1]ГУ Днепропетровская медицинская академия, Министерство здравоохранения Украины; [2]ГУ Днепропетровская областная клиническая больница им. И.И. Мечникова, Днепр; [3]Днепровский национальный университет им. О. Гончара, Украина

Цель исследования - определение отдаленной выживаемости больных сочетанным атеросклеротическим поражением церебральных и коронарных артерий, перенесших хирургическую реваскуляризацию обоих бассейнов.

Исследование функции выживания проведено в шести группах пациентов с сочетанным атеросклеротическим поражением церебральных и коронарных артерий, которым проведена реваскуляризация обоих бассейнов разными методами в различной последовательности и в различные сроки. В каждой группе проводили анализ функции выживаемости, начиная с 30 дня послеоперационного периода, используя оценку Каплана–Мейера. Сравнение функций выживаемости в разных группах проводили по логранговому критерию (logrank test) Сравнение функций выживаемости проводилось в группах пациентов, которым применены альтернативные методики реваскуляризации каротидного и коронарного бассейнов.

На протяжении первых 5 лет после проведения реваскуляризации каротидного и коронарного бассейнов функция выживаемости практически не отличалась у пациентов, которым проведены эндоваскулярные операции для реваскуляризации обоих бассейнов (стентирование церебральных и коронарных артерий) и гибридные операции (стентирование коронарных артерий+каротидная эндартерэктомия). В период 5-10 лет после оперативного вмешательства лучше выживали пациенты после гибридных операций (p=0,026). Основными причинами смерти пациентов явились кардиальные и церебральные события, незначительная часть пациентов умирала от других причин. Выживаемость пациентов на протяжении 10 лет после операции практически не отличалась при проведении стентирования церебральных артерий перед аорто-коронарным шунтированием и при симультантной операции каротидная эндартериэктомия+аорто-коронарное шунтирование (p=0,532).

რეზიუმე

მულტიფოკალური ათეროსკლეროზის მქონე ავადმყოფების გადარჩენა კაროტიდული და კორონარული აუზების ქირურგიული რევასკულარიზაციის შემდგომ

[2]ს.გრიგორუკი, [1,2]ა. სირკო, [1,2]ს. დუდუკინა, [3]ო.მაცუგა

[1]დნეპროპეტროვსკის სამედიცინო აკადემია, უკრაინა; [2]დნეპროპეტროვსკის ი.მეჩნიკოვის სახელობის საოლქო კლინიკური საავადმყოფო; [3]დნეპრის ო. გონჩარის სახელობის ეროვნული უნივერსიტეტი, უკრაინა

კვლევის მიზანს წარმოადგენდა გრძელვადიანი გადარჩენის შეფასება ავადმყოფებში ცერებრული და კორონარული არტერიების შერწყმული ათეროსკლეროზული დაზიანებით, რომელთაც ჩაუტარდათ ორივე აუზის ქირურგიული რევასკულარიზაცია.

გადარჩენის ფუნქციის კვლევა განხორციელდა პაციენტების ექვს ჯგუფში ცერებრული და კორონარული არტერიების შერწყმული ათეროსკლეროზული დაზიანებით, რომელთაც ორივე აუზის ქირურგიული რევასკულარიზაცია ჩაუტარდა სხვადასხვა მეთოდით, სხვადასხვა თანმიმდევრობით და სხვადასხვა ვადაზე. თითოეულ ჯგუფში გადარჩენის ფუნქციის ანალიზი კაპლან-მეიერის შეფასების გამოყენებით ჩატარდა პოსტოპერაციული პერიოდის 30-ე დღიდან. გადარჩენის ფუნქციის შედარება პაციენტების ჯგუფებში კაროტიდული და კორონარული აუზების რევასკულარიზაციით ალტერნატიული მეთოდიკების გამოყენებით ჩატარდა *logrank test* –ის კრიტერიუმით.

კაროტიდული და კორონარული აუზების რევასკულარიზაციის ჩატარებიდან პირველი 5 წლის განმავლობაში გადარჩენის ფუნქცია პაციენტებში, ვისაც ორივე აუზის რევასკულარიზაცია ჩაუტარდა ენდოვასკულური ოპერაციით (ცერებრული და კორონარული არტერიების სტენტირება) და პაციენტებში, ვისაც ჩაუტარდა ჰიბრიდული ოპერაცია (კორონარული არტერიების სტენტირება+კაროტიდული ენდარტერექტომია) პრაქტიკულად არ განსხვავდებოდა. ოპერაციული ჩარევიდან 5-10 წლის შემდეგ გადარჩენის მაჩვენებელი უკეთესი იყო ჰიბრიდული ოპერაციების შემდეგ (p=0,026). პაციენტების სიკვდილის ძირითად მიზეზებს კარდიალური და ცერებრული მოვლენები წარმოადგენდა,სხვა მიზეზების გამო გარდაიცვალა პაციენტთა უმნიშვნელო ნაწილი. აორტოკორონარული შუნტირების წინ ცერებრული არტერიების სტენტირებაჩატარებული პაციენტების და სიმულტანურ ოპერაციაჩატარებული (კაროტიდული ენდარტერექტომია+აორტოკორონარული შუნტირება) პაციენტების გადარჩენა ოპერაციის შემდეგ 10 წლის განმავლობაში პრაქტიკულად არ განსხვავდებოდა (p=0,532).