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V.V. Antonenko [1, 2 *], ***S.O. Dubrov*** [2]

NEUROPSYCHOLOGICAL INDICATORS OF POSTOPERATIVE COGNITIVE DYSFUNCTIONS AFTER OFF PUMP CORONARY ARTERY BYPASS GRAFTING

SI "National scientific center of surgery and transplantation named after O.O. Shalimov to National Academy of Medical Sciences of Ukraine" [1]
Academician Shalimov str., 30, Kyiv, 03126, Ukraine
[*]e-mail: antonenkovv93@gmail.com
Bogomolets National Medical University [2]
Beresteiskyi ave., 34, Kyiv, 01601, Україна
e-mail: sergii.dubrov@gmail.com
ДУ «Національний науковий центр хірургії та трансплантології ім. О.О. Шалімова Національної академії медичних наук України» [1]
вул. Академіка Шалімова, 30, Київ, 03126, Україна
Національний медичний університет ім. О.О. Богомольця [2]
пр. Берестейський, 34, Київ, 01601, Україна

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Ключові слова: *когнітивні дисфункції, коронарне шунтування на працюючому серці, нейрокогнітивне тестування, загальна анестезія*

Abstract. Neuropsychological indicators of postoperative cognitive dysfunctions after off-pump coronary artery bypass grafting. Antonenko V.V., Dubrov S.O. *The problem of postoperative cognitive dysfunctions (POCD) becomes more significant with the increase in frequency and expansion of operations in cardiac surgery practice. It's one of the common clinical complications following anesthesiologic support in cardiac surgery, which can change in a long-term period. POCD is a decrease of cognitive functions after surgery and general anesthesia from the baseline preoperative level. It's characterized by impairment of attention, concentration, memory, learning and processing of information, verbal, visual and visuospatial deficits. The attention of anesthesiologists and specialists in related specialties is attracted by the medical and social consequences of cognitive disorders, which have a negative impact on the duration of hospitalization, its cost, and the quality of life of patients in the remote postoperative period with an increase in the frequency and duration of incapacity for work, the need for rehabilitation, the financial burden on the patient and his family The aim of our study was to identify neuropsychological indicators of cognitive functions in the short-term and long-term postoperative period in patients with coronary heart disease who underwent off-pump coronary bypass grafting. There were examined 257 patients of 44-78 years old with coronary artery disease, all of them underwent off-pump coronary bypass grafting during period of 2019-2021 years and were hospitalized in the department of Cardiac Surgery at the National scientific center of surgery and transplantation named after O.O. Shalimov, Kyiv, Ukraine. Trail Making Test (TMT) and Mini Mental State Examination (MMSE) were used for cognitive function assessment. This study showed that 47.08% of patients had cognitive dysfunctions after cardiac surgery, which improved in postoperative period after 6 months in 19.01% (n=23) of patients with POCD. Worsening of cognitive performance was observed mainly in older population (65 and older). Geriatric patients had lower cognitive performance and are vulnerable to neuro-physiological changes after cardiac surgery, that may be a higher risk of POCD. The results of testing using MMSE and TMT in patients with coronary heart disease who underwent off pump coronary artery bypass grafting revealed that the frequency of POCD with a maximum decrease of cognitive functions was on the 3rd day after surgery with gradual recovery of cognitive functions on 6-8 day. However, in 80.99% of patients with POCD the level of cognitive functions is not recovered in full preoperative score.*

Реферат. Нейропсихологічні показники післяопераційних когнітивних дисфункцій після коронарного шунтування на працюючому серці. Антоненко В.В., Дубров С.О. *Проблема післяопераційних когнітивних дисфункцій (ПОКД) набуває все більшого значення зі збільшенням частоти та розширенням обсягів операцій у кардіохірургічній практиці. Це одне з поширених клінічних ускладнень після загальної анестезії в кардіохірургії, яке може змінюватися у віддаленому періоді. ПОКД – це зниження когнітивних функцій після операції та анестезії порівняно з базовим передопераційним рівнем. Характеризується погіршенням уваги, концентрації, пам'яті, навчання та обробки інформації, мовними, зоровими та візуально-просторовими порушеннями. Увагу*

анестезіологів і фахівців суміжних спеціальностей привертають медико-соціальні наслідки когнітивних розладів, які негативно впливають на тривалість госпіталізації, її вартість, якість життя пацієнтів у віддаленому післяопераційному періоді зі збільшенням частоти і тривалості непрацездатності, потребою в реабілітації, фінансовим навантаженням на пацієнта та його сім'ю. Метою нашого дослідження було визначення нейропсихологічних показників когнітивних функцій у найближчому та віддаленому післяопераційному періоді у хворих на ішемічну хворобу серця, які перенесли коронарне шунтування на працюючому серці. Обстежено 257 пацієнтів віком 44-78 років з ішемічною хворобою серця, які перенесли коронарне шунтування на працюючому серці в період 2019-2021 років та перебували на стаціонарному лікуванні у відділенні кардіохірургії Національного наукового центру хірургії та трансплантології ім. О.О. Шалімова, м. Київ, Україна. Дослідження когнітивних функцій виконували за допомоги тесту на встановлення послідовності цифр та літер (TMT) та короткої шкали дослідження психічного статусу (MMSE). Це дослідження показало, що 47,08% пацієнтів мали когнітивні дисфункції після кардіохірургічного втручання, які покращилися в післяопераційному періоді через 6 місяців у 19,01% (N=23) пацієнтів з ПОКД. Погіршення когнітивних функцій спостерігали переважно в пацієнтів старшого віку (65 років і старше). Пацієнти геріатричного віку мали нижчі когнітивні показники і були вразливими до нейрофізіологічних змін після кардіохірургічних втручань, що може бути причиною вищого ризику розвитку ПОКД. Результати тестування з використанням MMSE та TMT у пацієнтів з ішемічною хворобою серця, яким було проведено аортокоронарне шунтування на працюючому серці, показали, що частота розвитку ПОКД була з максимальним зниженням когнітивних функцій на 3-й день після операції та їх поступовим відновленням на 6-8 день. Однак у 80,99% пацієнтів з ПОКД рівень когнітивних функцій не відновлювався в повному обсязі до передопераційного показника.

The problem of postoperative cognitive dysfunctions (POCD) becomes more significant with the increase in frequency and expansion of operations in cardiac surgery practice. It's one of the common clinical complications following anesthesiologic support in cardiac surgery, which can change in a long-term period.

POCD is a decrease of cognitive functions after surgery and general anesthesia from the baseline preoperative level. It's characterized by impairment of attention, concentration, memory, learning and processing of information, verbal, language, visual and visuospatial deficits [1, 2]. According to duration, POCD can be classified into two types: short-term (cases of manifestations and persistence of cognitive disorders within 7 days of the postoperative period) and long-term (if cognitive disorders persist for more than 7 days/months/years). The incidence of early transitory cognitive decline, which is lasting up to 6 weeks after cardiac surgery, is 20-50%. [3]. The long-term cognitive dysfunctions can manifest as an insignificant deterioration, which occurs during 6 months after cardiac surgery with an incidence of 10-30% [2, 3]. Among risk factors of POCD – old age, preexisting cardiac, cerebral, and vascular diseases, intra- and postoperative complications [4]. A study demonstrated that female gender, old age and increased postoperative creatinine levels are more significantly associated with POCD development [5]. In a retrospective study Laalou et al. [6] described that POCD depended on age and time of observation. The incidence of cognitive dysfunction was in 23-29% patients aged 60-69 years and over 70 years in one week, and in 14% patients older than 70 years – 3 months after surgery. The risk of POCD in elderly patients [7] leads to a decrease in the quality of life and an increase in mortality [8]. A significant role is usually played by the irreversible nature of POCD, due to which developing of severe dementia can limits patients' ability and requires daily social and medical care.

The next important risk factor is cerebral hypoperfusion which contributes to postoperative brain damage, mostly in atherosclerotic patients [9]. Also, the incidence of POCD can be associated with cerebral inflammation because of neuronal injuries [10]. The literature review shows that surgical operation could trigger brain mast cell degranulation, activation of microglia and release of inflammatory cytokines. These changes can lead to neuronal damage and activation of neuronal apoptosis [11]. International retrospective studies demonstrated that the most common cause of POCD after cardiac surgery is coronary artery bypass with an incidence of 37.6% (7 days) and 20.8% (after 3 month) in postoperative period [12]. A significant amount of research concerns prevalence of POCD in patients who have undergone non-cardiac surgical interventions, while persistent POCD (7 days or more) is registered in 29% of patients, at the age under 65, the frequency of POCD in such interventions increased up to 30% [13], early POCD in this category of patients is registered in 47% [14]. Studies show that the incidence of POCD increases in patients with artificial blood circulation during surgery [15, 16, 17]. Therefore, the current theories of the POCD development in cardiac surgery have been updated and include risk factors associated with perfusion, patients and anesthesia [18]. Studies on the development of POCD and the recovery of cognitive function in the delayed period in patients after off-pump coronary bypass surgery demonstrate radically

different results [17, 19], which determines the relevance of this study.

International prospective studies, mainly International Study of Post Operative Cognitive Dysfunction – ISPOCD 2 (2000), demonstrate the frequency of postoperative cognitive deficits in 9,9% of patients, in elderly patients (75 years and older) – in 14% for more than 3 months, in 10,4% – during 1-2 years of the postoperative period, and after 2 years in only 1-2% of cases [20]. These data correspond to other previous studies, where Qiao Y. et al. [20] demonstrated, that in 7 days after the surgery with general anesthesia, cognitive dysfunctions were diagnosed in 19.2% of patients, and after 3 months – in 6.2%. Thus, it is shown that early cognitive dysfunction after surgical operations under general anesthesia in middle-aged patients is quite frequent, however, a tendency to decrease in POCD, according to neuropsychological testing, was observed during the first three months after surgery.

Cognitive deficit is measured using a series of neurocognitive tests. Testing may involve completing a questionnaire to examine memory, attention, motor function, speach, executive function, etc. [17]. A commonly used screening test for dementia is The Mini- Mental Status Examination (MMSE), which is also sometimes used to quantify POCD [21]. The MMSE value below 25 is regarded as POCD (normal score is 25 and higher) [22, 23]. For determining the POCD it is important to compare cognitive functions before surgery and adjust them to the age-related level. Also, it's possible to use the Cognitive Failures Questionnaire for evaluation of the cognitive status before and after operation [23].

The attention of anesthesiologists and specialists in related specialties is attracted by the medical and social consequences of cognitive disorders, which have a negative impact on the duration of hospitalization, its cost, and the quality of life of patients in the remote postoperative period with an increase in the frequency and duration of incapacity for work, the need for rehabilitation, the financial burden on the patient and his family [24, 25].

The aim of our study was to identify neuropsychological indicators of cognitive functions in the short-term and long-term postoperative period in patients with coronary heart disease who underwent off-pump coronary bypass grafting.

MATERIALS AND METHODS OF RESEARCH

There were examined 257 patients aged 44-78 years with coronary artery disease, all of them underwent off-pump coronary bypass grafting during period of 2019-2021 years and were hospitalized to the department of Cardiac Surgery at the National scientific center of surgery and transplantation named after O.O. Shalimov, Kyiv, Ukraine.

The research was approved by the Biomedical ethics committee of the Bogomolets National Medical University and was conducted in accordance with the written consent of the participants and in accordance with the principles of bioethics set forth in the Helsinki declaration for the Ethical Principles of Medical Research Involving Human Subjects and the Universal Declaration of Bioethics and Human Rights (UNESCO).

All patients underwent a preoperative examination (questionnaire survey, anthropometric measurements, objective examination, laboratory tests, electrocardiography, echocardiography, coronary ventriculography, ultrasound examination of main arteries and veins, duplex scanning of neck vessels, esophagogastroduodenofibroscopy) and standardized neurophysiological tests before surgery, 3 days, 6-8 days, and 6 months after surgery. The assessment included measures of attention-executive functions: Trail Making Test (TMT-A and TMT-B parts) and Mini Mental State Examination (MMSE) [7]. All diagnosed identified cognitive impairments belonged to the mild category, severe disorders (for example, stroke) were not noted in the study group.

Patients, who underwent any cardiosurgical or neurosurgical intervention during their lifetime, with hemodynamically significant stenoses of the carotid arteries, neurological disorders, alcohol or drug addiction, 6 months after hospital discharge, were excluded. Patients, who required long-term artificial lung ventilation or repeated thoracotomy for surgical reasons and those who, for any reason, refused to participate in the study directly were also excluded.

Provision of anesthesia was carried out according to the guidelines: general combined anesthesia with mechanical ventilation and an induction dose of thiopental Na (5 mg/kg), fentanyl (2-3 μg/kg), rocuronium bromide (1 mg/kg). For maintenance of anesthesia, we used sevoflurane 0.9 – 1 MAC. The total dose of fentanyl was 11.5 -18.0 μg/kg, bolus injection with rocuronium bromide was used as required.

All statistical analyses were performed using the software package IBN SPSS Statistics v. 23.0. The distribution of quantitative data was checked by the Kolmogorov-Smirnov test. Quantitative indicators were compared using Wilcoxon's T-test or Student's T-test. Statistically significant level was $p<0.05$. The quantitative data were presented in M±SD (M – average, SD square deviation). The qualitative data were described in absolute (n) or percent (%). To compare the absolute and relative frequencies of qualitative indicators, conjugation tables with evaluation according to Pearson's χ^2 criterion were used.

RESULTS AND DISCUSSION

The cognitive dysfunctions were determined in early postoperative period in 121 patients (47.08% of operated ones). Demographic characteristics of the patient groups are shown in Table 1. In the total number of patients, the majority were men 73.54% (n=189), women – 26.46% (n=68). The distribution by gender in the group with POCD was identical: 76.86% of men (n=93) and women – 23.14% (n=28), (p<0.05).

Table 1

Demographic characteristics of the study population

Characteristics	Patients (n=257)	Patients with POCD (n=121)	p-value
Men	73,54% (n=189)	76,86% (n=93)	p<0,05
Women	26,46% (n=68)	23,14% (n=28)	p<0,05

There were revealed statistically significant differences in cognitive functions that arose and developed after surgical intervention, which were recorded in the early and remained in the long-term postoperative period.

Preoperative and postoperative test scores of patients with POCD are presented in Table 2.

Patients of the study group scored 27.49±2.19 points in preoperative testing on the MMSE scale. On the 3rd day after the operation, a significant decrease of the index to 22.81±1.51 points (p<0.05) was observed, which is by 17.02% less than the initial data. On the 6-8th day after the operation, the patients gained 24.62±1.74 points, which is by 10.44% lower than the preoperative values (p<0.05). At the same time, according to the interpretation scale, the cognitive status is described as mild cognitive impairment; 6 months after hospital discharge patients scored 25.32±2.36 points, which is still reliably (p<0.05) below the initial, preoperative level of cognitive status.

Table 2

Preoperative and postoperative test scores of patients with cognitive dysfunction

Test	Preoperative	3rd day follow -up	6-8 day follow- up	6 months follow- up	p-value
MMSE (score)	27.49±2.19	22.81±1.51	24.62±1.74	25.32±2.36	p<0.05
TMT-A (seconds)	26.36±1.59	37.21±2.15	33.71±3.32 s	31.31±2.33	p<0.05
TMT-B (seconds)	68.19±2.21	77.31±2.23	73.44±2.32	70.12±2.24	p<0.05

The results of the TMT-A showed that on an average the patients spent 26.36±1.59 seconds on performing the test in the preoperative period, on the 3rd day the score was higher by 41.16% (37.21±2.15 second), and on the 6th-8th day it was 33.71±3.32 seconds, that is by 27.88% longer than the initial level. However, 6 months after the operation, the test results improved and amounted to 31.31±2.33 seconds, which is by 18.78% more than the initial preoperative indicator (p<0.05).

The second part of the TMT (part B) showed similar results: before surgery patients spent 68.19±2.21 seconds, on the 3rd day it was higher – 77.31±2.23 seconds, on days 6-8 – 73.44±2.32 seconds, the growth rate was 13.37% and 7.7%, respectively (p<0.05). After 6 months TMT-B was by 2.83% more (70.12±2.24 seconds), i.e., reliably close to the value of the preoperative indicator (p≥0.05).

This study shows that 47.08% of patients had cognitive dysfunctions after cardiac surgery, which improved in postoperative period after 6 months in 19.01% (N=23) of patients with POCD. Neuropsychological changes were identified mostly in men – 76.86% of patients. Worsening of the cognitive performance was observed mainly in older population (65 and older). Geriatric patients have lower cognitive performance and are vulnerable to neurophysiological changes after cardiac surgery, that may be a higher risk of POCD [26, 27]. Study shows that in older patients the prevalence of dementia in several years after cardiac surgery is increased [28]. That's

why it would be necessary to optimise early detection of cognitive impairment and follow-up of patients with a high risk of progression of dementia after cardiac surgery [29].

CONCLUSION

1. The results of testing using Trail Making Test and Mini Mental State Examination in patients with coronary heart disease who underwent off-pump coronary artery bypass grafting revealed that the frequency of postoperative cognitive dysfunction with a maximum decrease of cognitive functions was on the 3rd day after surgery and their gradual recovery on 6-8 day.

2. In 80.99% of patients with postoperative cognitive dysfunction the level of cognitive functions does not recover in full preoperative score after six months.

Contributors:

Antonenko V.V. – conceptualization, investigation, writing – original draft, visualization;

Dubrov S.O. – conceptualization, writing – review & editing, project administration, supervision.

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