

Original Article**Prevention of Cognitive Frailty in Patients of Older Age Groups after Open-Heart Surgery under Cardiopulmonary Bypass****Orobtsova, M¹*, Gorelik, S¹, Belousova, O¹, Avdeeva, I¹, Krupenkina, L¹***1. Belgorod State University, Belgorod, Russia (85 Pobedy Street, Belgorod, 308015)*Received 26 December 2021; Accepted 15 January 2022
Corresponding Author: ozakramgh@gmail.com**Abstract**

Acute change in mental state is characterized by an impaired level of consciousness, decreased attention, and cognitive changes, and has a variable course throughout its period. Delirium is common in the elderly and hospitalized patients, especially after major surgeries, and increases mortality and morbidity in patients. This study was designed to investigate the relationship between the incidence of delirium after heart surgery and some intrusive factors during surgery. A total of 263 middle-aged, elderly, and chronic patients with functional class III-IV heart failure were classified based on the New York Heart Association classification and valvular heart disease. Cognitive impairment screening was performed using the Mini-Cog test and clock drawing test in addition to standard general clinical examinations on patients. Cognitive impairment was diagnosed in patients with coronary heart disease preparing for planned surgical treatment, regardless of age, while the results of both tests were significantly worse in elderly patients than in their middle-aged counterparts. In the early postoperative period, both among the middle-aged and elderly patients, there was a significant improvement in the results of the clock drawing test. Middle-aged patients also showed improved results on the Mini-Cog test, while the elderly patients showed an increase in cognitive dysfunction. In the third stage of the examination of cognitive function in the two studied groups of patients with valvular pathology at the first checkpoint, no statistically significant differences were found in the Mini-Mental State Examination (MMSE), Mini-Cog, and clock drawing test. The results of the clock drawing test in the main and control groups were recorded at 8.9 ± 0.4 and 5.8 ± 0.3 points, respectively ($P < 0.05$). The MMSE results were estimated at the points of 27.1 ± 0.1 and 24.1 ± 0.2 in the main and control groups, respectively, while the results of the Mini-Cog test were calculated at 2.2 ± 0.2 and 1.2 ± 0.4 words in the main and control group, respectively ($P < 0.05$). The application of the algorithm for the prevention of cognitive frailty in patients of older age groups after open-heart surgery under cardiopulmonary bypass would possibly lead to a decrease in the number of early and late postoperative complications, which shows the necessity of using it for patients of older age groups in multimodal programs to prepare them for surgical interventions.

Keywords: Cardiac surgeries, Cardiopulmonary bypass, Chronoblockers, Cognitive disorders, Metabolomics**1. Introduction**

With the advancement of technology and urban life, the incidence of coronary heart disease is increasing in the world. It is estimated that approximately 500,000 coronary artery bypass graft (CABG) surgeries are performed annually in the United States (1).

Cardiovascular diseases are one of the most important and the leading causes of death in different societies (2). Various methods and treatments have been developed for the treatment of cardiovascular diseases (3). One of the most important invasive treatments is heart surgery, which is performed for various purposes.

Today, heart surgeries are increasingly performed around the world, including CABG and valve replacement surgeries (4). Like other surgeries and invasive procedures, heart surgeries are also performed. They can be associated with complications and problems that are life-threatening not only during but also after the surgery (5). In these operations, the coagulation system is altered: therefore, such risks as bleeding during and after the surgery are among the most important and serious complications of heart surgery. Pericardial effusion, which is due to the accumulation of fluid around the heart, has also been considered an important and common complication of heart surgery in previous studies. Sickness or subsequent problems and complications increase significantly after heart surgery (6).

Despite providing intensive care to patients after heart surgery, some complications are inevitable following any heart surgery. These complications can increase the costs of treatment and length of hospital stay and in some cases even lead to the death of patients. Complications and problems after cardiac surgery are mainly due to underlying diseases and fever due to surgery. The most important of these complications include electrolyte disturbance, gas exchange disturbance, myocardial infarction, renal failure, bleeding, and neurological complications (7).

Neurological complications are one of the most prevalent problems following heart surgery, which can include cognitive deficits. Delirium is one of the most common cognitive complications in these patients and is a syndrome characterized by impaired consciousness and changes in cognition. However, the source adds that delirium is not only less commonly diagnosed in intensive care units but is also associated with long-term hospitalization, high costs, and even high mortality in intensive care units (8).

The results of a study by Ebert, Walzer (9) showed that neuropsychological disorders after heart surgery might be associated with transient hypoxia and subsequent temporal lobe disorder. In a study by Hofsté, Linssen (10), the risk factors for postpartum

delirium were listed as age 70 years or older, female gender, and intraoperative hemoglobin less than 5 mmol. Other predisposing causes of postoperative cognitive impairment include the duration of cardiopulmonary bypass (greater than or equal to 2.5 h) and the duration of aortic clamping (more than 70 min).

In connection with the increasing aging of the population worldwide, there is a need to search for ways to improve the quality of life of patients with cardiac surgery pathology, especially in elderly and senile people (11). Cognitive dysfunction is a frequent consequence of cardiac surgery and is caused by several factors, including macroembolization of cerebral vessels, transient cerebral ischemia due to cerebral hypoperfusion when using cardiopulmonary bypass, the development of systemic inflammatory reaction, and brain edema (12, 13). The duration of the surgical intervention and the features of the used anesthetic agents significantly affect the cognitive abilities of cardiac surgery patients. In elderly and senile patients with comorbid pathology, it significantly aggravates the process of postoperative rehabilitation, leading to disability (14), which, on the one hand, is not economically profitable, and on the other hand, worsens the functional status and reduces the quality of life of patients. All these reasons highlight the necessity to improve not only the methods of cardiac surgical treatment but also preoperative preparation and postoperative management of patients in older age groups.

The number of publications showing that nutraceuticals and herbal medicines have antioxidant (14, 15), anti-inflammatory, and anti-amyloid properties is increasing every year. They can regulate mitochondrial stress (16), the activity of antioxidant systems, the activity of neurotrophic factors, and factors of apoptosis; that is, they can influence the main mechanisms of brain aging (17).

This study aimed to develop an algorithm for the diagnosis and prevention of cognitive impairment in the early and late postoperative periods in patients of older age groups who underwent open-heart surgery and cardiopulmonary bypass.

2. Materials and Methods

In this experiment, with planning and arrangement, the work was conducted as an open and controlled study. A total of 263 middle-aged, elderly, and chronic patients with functional class III-IV heart failure were classified based on the New York Heart Association (NYHA) and valvular heart disease (severe aortic stenosis, grade III-IV mitral regurgitation).

In the first phase of the experiment, 200 middle-aged and elderly patients were investigated, and their mean age was estimated at 60.3 ± 10.3 years. All patients in the first stage were divided into the following groups. The first group consisted of 85 patients who underwent coronary artery bypass graft surgery under open cardiopulmonary bypass. The second group involved 115 patients who underwent cardiopulmonary bypass valve replacement surgery in "open heart". Each group was divided into two subgroups. As a result, the groups were formed as follows: Group 1.1 - Middle-aged patients who underwent open-heart coronary artery bypass graft surgery ($n=42$, mean age= 51.3 ± 5.6 years), Group 1.2 - Elderly patients who underwent cardiopulmonary bypass coronary artery bypass graft surgery ($n=43$, mean age= 65.4 ± 4.8 years), Group 2.1 - Middle-aged patients who underwent open-heart valve replacement cardiopulmonary bypass surgery ($n=52$, mean age= 50.3 ± 9.6 years), and Group 2.2 - Elderly patients who underwent open cardiopulmonary bypass surgery ($n=63$, mean age= 68.3 ± 7.3 years).

Cognitive impairment screening was performed using the Mini-Cog test and clock drawing test in addition to standard general clinical examination on patients who had been referred to the outpatient clinic of the Heart Surgery Center of Belgorod St. Joseph Regional Hospital, Russia, before surgery. After surgical treatment, their condition was stabilized on day 2.7 ± 7 . If the patient could not repeat 3 words, the Mini-Cog test was not performed, and the clock drawing test scored 14 or less. In the second phase of the study, based on the obtained data, a program was developed to prevent cognitive impairment in patients in older age

groups after open-heart surgery under cardiopulmonary bypass, and in the third phase, a proposed program was performed to prevent cognitive impairment in patients with chronic heart failure in the early and late postoperative periods by evaluating its effectiveness.

2.1. Inclusion Criteria

1. Availability of the patient's informed consent to participate in the study.
2. Patient compliance.
3. Living with family (possibility of monitoring by and assistance from the family).
4. Presence of monovalve pathology (severe aortic stenosis, mitral insufficiency of degree III-IV), revealed by echocardiographic examination, chronic heart failure according to the NYHA classification of functional class III-IV.
5. Absence of cerebrovascular accident in patient's medical history.
6. Stability of hemodynamics during the patient's admission to the hospital.
7. The Mini-Mental State Examination (MMSE) score of 24-27, corresponding to moderate cognitive impairment.
8. Duration of anesthesia: 5 ± 2.5 h.
9. Duration of surgery: 6 ± 2.5 h.
10. Duration of perfusion: 118 ± 20 min.
11. Duration of aortic compression 70 ± 20 min.

2.2. Exclusion Criteria

1. Absence of the patient's informed consent to participate in the study.
2. Patient noncompliance.
3. Living alone.
4. Definite cognitive impairment (MMSE score of below 24-27) associated with concomitant pathology, including chronic cerebral ischemia.
5. Duration of anesthesia: more than 5 ± 2.5 h.
6. Duration of surgery: more than 6 ± 2.5 h.
7. Duration of perfusion: more than 118 ± 20 min.
8. Duration of aortic compression: more than 70 ± 20 min.
9. Presence of complex heart defects.

10. Presence of chronic non-specific lung diseases.
11. Unstable hemodynamics at any stage of surgical treatment and in the postoperative period.
12. Presence of concomitant acute inflammatory, infectious, oncological, immunocomplex diseases.
13. Presence of chronic diseases in the acute phase.
14. Pericardial pathology.
15. Cardiomyopathy.

2.3. Checkpoints of the Patients in the Main and Control Groups

2.3.1. First Point

When contacting the outpatient clinic of the cardiac surgery center, a cardiological examination was carried out to determine the indications for the surgical intervention, and a screening examination of cognitive functions was conducted (Mini-Cog test and the clock drawing test). Patients with ischemic heart disease and valvular heart diseases were examined.

2.3.2. Second Point

The patients were examined in the outpatient clinic of the cardiac surgery center 45 ± 4.4 days before the surgical treatment; patients with valvular pathology were evaluated. The patients underwent cardiological examination, MMSE test, standard clinical diagnostic examination, and additional examinations (i.e., potassium, sodium, magnesium, chlorine, selenium, calcium, vitamin B₁₂, protein S100). The patients of the main group were provided the developed program for the prevention of cognitive frailty.

2.3.3. Third Point

The patients were examined in the cardiac surgery hospital on day 7 ± 2.3 after the surgical treatment of valvular heart disease under cardiopulmonary bypass. A cardiological examination and an examination of cognitive functions, using the Mini-Cog test and MMSE, were performed. Moreover, the patients underwent standard and additional clinical diagnostics. On the day of discharge, a conversation was held with the patients and families on the management of the patients after discharge from the hospital, and written recommendations were given out.

2.3.4. Fourth Point

The patients were examined in the outpatient clinic of the cardiac surgery center on day 30 ± 2.1 after the surgery. A cardiological examination and an examination of cognitive functions (i.e., Mini-Cog test and MMSE) were performed. Furthermore, the patient underwent a planned standard and additional clinical and diagnostics examinations. The diary entries were monitored, and recommendations for further maintenance were given when required.

2.3.5. Fifth Point

The postoperative patients were examined on day 180 ± 10.6 in the outpatient clinic of the cardiac surgery center. A cardiological examination, an examination of cognitive functions, a clinical diagnostic examination, and an analysis of keeping the diary were carried out. Patients were given recommendations for further cognitive stimulation.

2.4. Cognitive Stimulation of Patients

Reminiscence psychotherapy (memory psychotherapy) is a technique that is used to help people remember events from their past using reminders. The patients and their families were asked to gather once a week in a family circle, share memories from the past, and illustrate them with family photo albums. Every morning or the night before, the patient made a written plan for the current day with an approximate determination of the time frames. Every day after reading or watching the news, the events were discussed in the family circle. Every day in the evening, the patients, by themselves or with the help of family, carried out an analysis of the last day.

Reality orientation is an opportunity for people to connect with the real time employing written and verbal reminders of past and present life events. The patients and their families were asked to discuss such topics as weather and current memorable events during a daily walk. Three times a week for 10-15 minutes, the patients were offered various cognitive stimulation activities. In this regard, patients who had a computer were offered to take cognitive stimulation tests online

(e.g., on the website of www.experimental-psyhic.ru). The rest of the patients were given materials with tests for cognitive stimulation, including the Schulte test, the Gorbov-Schulte test, and the Stroop test.

The patients were asked to describe the quality of sleep every day in the diary, which included the number of awakenings during the day and night hours. An example of the patient’s diary is shown in table 1.

Table 1. Example of the patient’s diary

Date				
Reminiscence psychotherapy	+	+	+	+
Orientation to reality	+	+	+	+
Analysis of the past day	+	+	+	+
Preparing a plan for the day and monitoring its completion	+	+	+	+
Reading the news or watching TV programs with discussion (instead of watching TV passively)	+	+	+	+
Mastering new computer programs, doing test online or using handed out materials	+		+	
Sleep monitoring	+	+	+	+
Sleep during day (awakenings number)	-	1	1	1
Sleep during night (awakenings number)	1	1	2	1
Brain exercises		+		+
Correction of diet	+	+	+	+
Medically induced correction	+	+	+	+

The patients, independently or accompanied by family members, performed “brain exercises” three times a week for 15 min; for example, they did mirror painting and finger gymnastics within 30 seconds or showed zero and a "bunny" on different hands and simultaneously changed the “bunny” to zero and zero to “bunny”, which improved interhemispheric connections.

The diet of patients, which was developed by the clinical recommendations for the perioperative management of elderly and senile patients, was prepared by the Ministry of Health of the Russian Federation (Moscow, 2018) and included foods with a

high content of microelements, vitamins, and amino acids and lacked foods that would lead to protein-energy malnutrition and various disorders in the form of cognitive deficit and dementia, such as postoperative delirium, disorientation in space, psychoemotional agitation, anxiety and depression, disturbance of the sleep-wake cycle, and impaired cerebral circulation.

It used the original preparation of Cerebrostim containing taurine and guarana (*Paullinia cupana*) extract (1 pill/day for 1 month before surgery, and one pill/day for 2 months after discharge from the hospital) to correct the nutritional status, improve memory, stimulate mental processes, and reduce chronic fatigue and stress tension. The patients’ families were asked to monitor the use of standard drug therapy daily, according to the clinical guidelines for the perioperative management of elderly and senile patients developed by the Ministry of Health of the Russian Federation (Moscow, 2018), and additional therapies.

The effectiveness of the program presented in this study to correct cognitive impairment in elderly patients was evaluated by the dynamics of neuropsychological tests. These tests included clock drawing, Mini-Cog, and MMSE tests; the analysis of complications in the early, late, and long stages, dynamics of blood biochemical composition, S100 calcium binding protein B (S100B) protein indices, without calcium and ionization, magnesium, selenium, vitamin B₁₂; evaluation of lipid profile and coagulation system; and evaluation of several medical and economic indicators (i.e., postoperative delirium, spacelessness, emotional arousal, anxiety, depression, sleep-wake cycle disorders, and acute cerebrovascular events).

Mathematical and statistical processing of the research results was carried out using the student's t-test and the ϕ^* criterion (Fisher's transformation). The student's t-test was used to identify significant differences between the quantitative characteristics of the studied processes. The ϕ^* criterion was employed when comparing samples for a qualitatively determined attribute.

3. Results

In the first step, when studying cognitive functions, the following results were obtained. Cognitive dysfunctions were present in patients with valvular heart disease who were preparing for planned surgical treatment, both in the middle-aged and elderly, according to the results of both tests. In the early postoperative period in middle-aged patients, no reliable evidence of exacerbation of cognitive impairment was found. However, in elderly patients, the exacerbation of cognitive impairment was reliably observed in the early postoperative period (Table 2).

Cognitive impairment was diagnosed in patients with coronary heart disease preparing for planned surgical treatment, regardless of age, while the results of both tests were significantly worse in the elderly patients than in the middle-aged patients. In the early postoperative period, both among the middle-aged and elderly patients, there was a significant improvement in the results of the clock drawing test. Middle-aged patients also showed improved results on the Mini-Cog test, while the elderly patients showed an increase in cognitive dysfunction according to the results of the Mini-Cog test (Table 3).

Table 2. Results of the examination of the middle-aged and elderly patients with valvular heart disease

Age	Clock drawing test (mean score)		Mini-Cog test (mean score)	
	Before surgery	After surgery	Before surgery	After surgery
Middle-aged patients	6.80±0.70	6.80±0.70	2.50±0.10	2.30±0.70
Elderly patients	6.30±0.20*	5.30±0.20***	1.80±0.20*	1.40±0.10***

* $P<0.05$ between groups, ** $P<0.05$ within the group

Table 3. Results of the examination of the middle-aged and elderly patients with ischemic heart disease

Age	Clock drawing test (mean score)		Mini-Cog test (mean score)	
	Before surgery	After surgery	Before surgery	After surgery
Middle-aged patients	6.70±0.40	7.10±0.70**	1.70±0.70	2.10±0.10**
Elderly patients	7.20±0.80*	7.50±0.50***	2.10±0.10*	1.60±0.40***

* $P<0.05$ between groups, ** $P<0.05$ within the group

In the third stage of the examination of cognitive function in the two studied groups of patients with valvular pathology at the first checkpoint, no statistically significant differences were found in the MMSE, Mini-Cog, and clock drawing test.

In the early postoperative period, when examining patients with valvular pathology on day 7±2.3 after surgery, compared to the control group, statistically significant results were shown by both the clock drawing test (8.6±0.1 and 6.9±0.4 points in the main and control groups, respectively, $P<0.05$) and MMSE (26.1±0.2 and 24.4±0.2 points in the main and control groups, respectively, $P<0.05$). The Mini-Cog test was not sensitive at this stage.

In the late postoperative period, on day 30±2 after surgical treatment, when evaluating patients with valvular pathology, an improvement in the test results was reliably diagnosed for all three performed tests, namely MMSE, Mini-Cog, and clock drawing test. The clock drawing test in the control and main groups scored 5.1±0.1 and 9.1±0.2 points, respectively ($P<0.05$); the results of MMSE were obtained at 19.7±0.2 and 26.1±0.2 points in the control and main groups, respectively ($P<0.05$); Mini-Cog test results were calculated at 3.0±0.1 and 1.3±0.2 words in the control and main groups, respectively ($P<0.05$).

In the distant period, the half-life results were achieved with long-term storage of the achieved results,

with daily cognitive stimulation. The results of the "Lesson test" were obtained at 8.9 ± 0.4 points in the primary group and 5.8 ± 0.3 points in the control group ($P < 0.05$), MMSE at 27.1 ± 0.1 points in the base group and 24.1 ± 0.2 points in the control group ($P < 0.05$), Mini-Cog test at 2.2 ± 0.2 words in the core group and 1.2 ± 0.4 words in the control group ($P < 0.05$) daily data on 2.3. The results of long-term preservation of the achieved results were obtained with daily cognitive stimulation, accounting for 8.9 ± 0.4 and 5.8 ± 0.3 points in the main and control group, respectively ($P < 0.05$) for the clock drawing test, 27.1 ± 0.1 and 24.1 ± 0.2 points in the main and control groups, respectively ($P < 0.05$) for MMSE, and 2.2 ± 0.2 and 1.2 ± 0.4 words in the main and control groups, respectively ($P < 0.05$) for Mini-Cog test. Data are presented in figures 1 and 2.

The dynamics of the metabolites analysis results in patients of the main and control groups are presented in tables 4 and 5. In the early postoperative period, there was a significant increase in S100B both in the main and control groups with the normalization of indicators (6 months after the surgery). The indicators of the levels of magnesium and selenium in the blood significantly increased after 6 months of the surgery. Indicators of the level of vitamin B12 significantly boosted starting 30 days after the surgical treatment. There were diagnostically significant reductions in cholesterol levels in the early postoperative period and persisted for 6 months of follow-up. Significant thrombocytopenia was diagnosed in the first week after the surgery, and platelet levels normalized 180 days after the treatment.

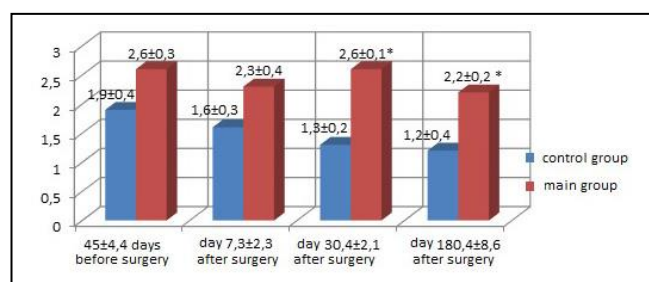


Figure 1. Comparative analysis of the Mini-Cog test results at all stages of the research
* $P < 0.05$ between groups, ** $P < 0.05$ within the group

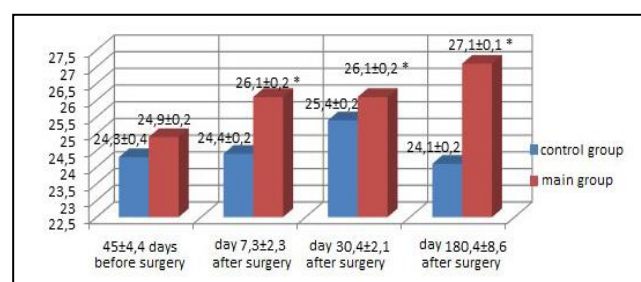


Figure 2. Comparative analysis of the MMSE test results at all stages of the research
* $P < 0.05$ between groups, ** $P < 0.05$ within the group

Table 4. Dynamics of the blood metabolites analysis results

Indicator	Before surgery	On day 7.3±2.3 after surgery	On day 30.4±2.1 after surgery	On day 80.4±8.6 after surgery
S100B (µg/l)	0.105±0.10	1.50±0.60*	0.407±0.10*	0.105±0.10
Ca ⁺⁺ (mmol/l)	2.0±0.40	2.40±0.60	2.20±0.50	2.30±0.40
Ca ⁺⁺ (ionized) (mmol/l)	0.80±0.50	1.00±0.80	1.00±0.50	1.20±0.60
Mg ⁺ (mmol/l)	0.60±0.20	1.20±0.20	1.10±0.10	1.20±0.20*
Selenium (µg/ml)	0.08±0.07	0.075±0.09	0.13±0.05*	0.18±0.30*
B ₁₂ (pg/ml)	594.20±0.60	300.30±0.40*	520.20±0.20*	650.60±0.40*
Total cholesterol (mmol/l)	5.10±0.80	3.40±0.30*	3.10±0.20*	2.70±0.30*
Platelets(×10 ⁹ /l)	210.30±50	90.40±10.00	190.80±40.00	208.20±0.00

* $P < 0.05$ between checkpoints

S100B: S100 calcium binding protein B

Table 5. Dynamics of the blood metabolites analysis results in patients in the control group

Blood test	Before surgery	On day 7±1 after surgery	On day 30±5 after surgery	6 months±10 days after surgery
S100B (µg/l)	0.108±0.10	1.50±0.50*	0.607±0.20*	0.205±0.10*
Ca ⁺⁺ (mmol/l)	1.95±0.60	2.00±0.40	2.10±0.30	1.75±0.30
Ca ⁺⁺ (ionized) (mmol/l)	0.90±0.54	1.10±0.40	1.00±0.50	0.95±0.40
Mg ⁺ (mmol/l)	0.70±0.30	1.40±0.70	1.00±0.10	1.00±0.20
Selenium (µg/ml)	0.08±0.05	0.075±0.09	0.1±0.05	0.16±0.04*
B ₁₂ (pg/ml)	580.10±0.20	175.20±0.10	528.30±0.20	512.10±0.20
Total cholesterol (mmol/l)	5.30±0.60	3.60±0.20*	3.40±0.20*	3.10±0.60*
Platelets (*10 ⁹ /l)	217.10±70.30	86.20±40.50*	176.40±90.10	214.40±90.40

* $P<0.05$ between groups, ** $P<0.05$ within the group
S100B: S100 calcium binding protein B

The assessment of medical and economic indicators, such as postoperative complications (i.e., postoperative delirium, disorientation in space, psychoemotional agitation, anxiety, depression, disturbance of the sleep-wake cycle, acute cerebrovascular accident) revealed 34.3 % and 12.9% increases in postoperative delirium ($P<0.05$) and 43.7% and 19.3% rises in the episodes of acute cerebrovascular accident ($P<0.05$) in the control and main groups, respectively. After 6 months, an increase in depression and anxiety was reliably demonstrated in the control group, compared to the main group (84.3% vs. 64.5%, $P<0.05$). The data is depicted in figure 3.

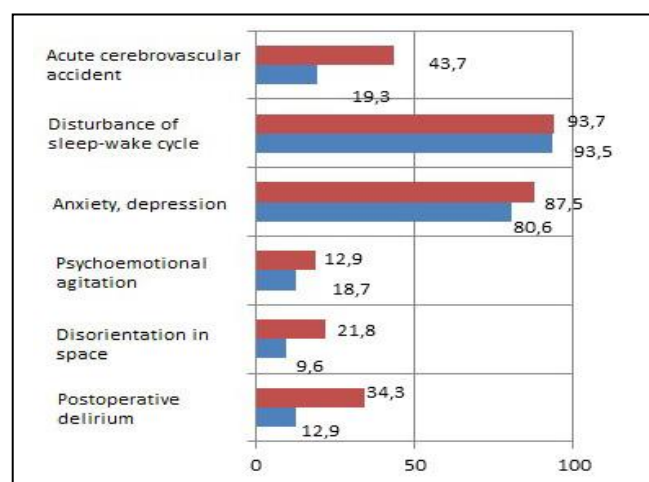


Figure 3. Dynamics of complications indicators in the postoperative period in the main and control groups

* $P<0.05$ between groups, ** $P<0.05$ within the group; red: the control group, blue: the main group

4. Discussion

Middle-aged and elderly patients with valvular pathology showed cognitive dysfunction according to the results of screening methods performed before the surgery. At the same time, the results of screening methods showed significantly lower indicators in the elderly people, compared to the middle-aged patients. There was a significant deterioration in cognitive dysfunction in the elderly patients according to the results of the clock drawing test from 6.3±0.2 to 5.3±0.2 points ($P<0.05$) in the early postoperative period. It was revealed that our proposed algorithm for the diagnosis and prevention of cognitive frailty in the early and late postoperative periods in people of older age groups could significantly reduce the percentage of early postoperative complications, such as postoperative delirium (from 34.3% to 12.9%) and acute cerebrovascular accident (from 43.7% to 19.3%), and late complications in the form of a decrease in anxiety and depression from 84.5% to 67.7%. It should be noted that the patients of the main group showed a more rapid normalization of the S100B protein, the level of total cholesterol, and platelets to a greater extent due to receiving hypolipidemic and dual antiplatelet therapy.

Calprotectin is a heterodimer protein and can bind to calcium and zinc (18). This protein is present in the cytosol of neutrophils and the membrane of monocytes.

Following the activation of neutrophils or binding of monocytes to the endothelium, calprotectin is released, whose level in serum or body fluids is an important indicator of inflammation (19). Calprotectin exerts both a bacteriostatic and a cytotoxic-like effect at the site. The physiological roles of this protein are not well understood and extensive research is being performed in prestigious laboratories around the world. The amount of this protein is normal in irritable bowel syndrome, however, it increases in Crohn's disease, ulcerative colitis, and colon cancer. If the level of calprotectin in the stool is low, it is unlikely that there is an inflammatory disease in the internal organs.

Magnesium prevents the coronary arteries from spasming, which is what causes severe chest pain called angina. Magnesium deficiency is the most common cause of arterial spasms. Electrolyte disorders, including hypomagnesemia, are one of the causes of cardiac arrhythmias after surgery (20). Magnesium deficiency is a relatively common electrolyte disorder in hospitalized patients that may be associated with arrhythmias, and arrhythmias due to magnesium deficiency may be resistant to antiarrhythmic medications and cardioversion. As a result, adding a magnesium sulfate diet to compensate for this deficiency is a way to prevent arrhythmias (21). Therefore, changes in the number of elements and vitamin B₁₂ can be due to their application in the medication regimen of patients.

Although it is not clear exactly how sleep can be beneficial to the body, sleep has always been mentioned as one of the most basic human needs (22). Each person's specific need for sleep is different. Cellular repair, comfort, relaxation, and physical-mental rest are established during sleep, and in fact, sleep is a restorative mechanism that helps the physical and mental reconstruction of humans. The results of various studies, along with a decrease in the quantity and quality of sleep of patients admitted to hospitals, have shown that patients in acute wards have identified sleep disorders as an important and major source of

stress during their hospitalization, which is caused by various individual or environmental factors. In a study, during 5 days after open-heart surgery, it was found that although there was no significant change in the quantity and duration of sleep of patients and even in some cases the percentage of daytime sleep increased from 45% to 60%, due to frequent interruptions (23) in the sleep rhythm during the first 3 days, sleep quality decreased.

The results of various studies have indicated that CABG harms all stages of sexual function. In this regard, the findings of a study conducted by Mourad, El Ghanam (24) in Egypt (2017) revealed that sexual function decreased up to 3 months after CABG. Likewise, the results of a study by some researchers in Iran (2019) showed a significant reduction in sexual function (25). Six months after CABG confirms in all respects. Accordingly, it can be acknowledged that one of the educational needs of patients after myocardial infarction is how to perform sexual activity. Regarding, it is recommended that issues related to sexuality and marital relations be part of the medical care topics for cardiovascular patients, necessary information be provided to patients in this regard, and patients and their spouses receive consultant in this area to reduce their stress.

Various studies have examined anxiety and depression before CABG (26). In some studies, the prevalence of pre-operative anxiety (40.27% to 27%) and pre-operative depression (-16% to 43%) has been reported (27). In a study carried out by Krannich, Weyers (28) in Germany (2007), using the Hospital Anxiety and Depression Scale, anxiety and depression occurred 2 days before and 10 days after exercise. The prevalence rate of depression was reported to be 25.8% and 17.5% before and after coronary artery disease, respectively, and that of anxiety was found to be 34% and 24.7% before and after surgery, respectively, and the relationship was significant and negative. According to the findings of another study, the prevalence of depression was 47% before CABG and

61% after that. In another study (2016), depression in patients undergoing heart surgery was reported at 17.1%. Major depression was similarly reported in a study conducted in 2015. The results of a study by Powell (2017) indicated that more than one-third of patients (35.9%) reported moderate to severe symptoms of depression on the basis of a questionnaire. Findings show that patients with depression before CABG also experience depression for a longer period.

The algorithm developed by us for the prevention of cognitive frailty in patients of older age groups after open-heart surgery under cardiopulmonary bypass showed that it was possible to achieve a decrease in the number of early and late postoperative complications, which showed the necessity of using it for patients of older age groups in multimodal programs to prepare them for surgical interventions.

Authors' Contribution

Study concept and design: M. O.

Acquisition of data: S. G.

Analysis and interpretation of data: O. B.

Drafting of the manuscript: I. A.

Critical revision of the manuscript for important intellectual content: L. K.

Statistical analysis: M. O.

Administrative, technical, and material support: S. G.

Ethics

The human study was approved by the Belgorod State University, Belgorod, Russia.

Conflict of Interest

The authors declare that they have no conflict of interest.

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