Bi BIOMEDICINSKA ISTRAŽIVANJA
2022;13(1):11–19

UDK: 616-089.168:616.345:616-006
DOI: 10.5937/BII2201011B

Original article

Effect of perioperative blood loss on cognitive function disorders after colon cancer surgery

Dalibor P. Bošković[1], Sanja S. Marić[2], Marko B. Kovačević[1], Bojan R. Golijanin[1]

[1]PHI Hospital "Serbia" East Sarajevo, The Republic of Srpska, Bosnia and Herzegovina

[2]2University Hospital Foca, The Republic of Srpska, Bosnia and Herzegovina

Primljen – Received: 18/10/2021
Prihvaćen – Accepted: 10/05/2022

Corresponding author:
Dalibor Bošković, MD
Spasovdanska broj 39,
71123 East Sarajevo
dalibor73bos@yahoo.com

Summary

Introduction. Postoperative cognitive dysfunction (POCD) is very common in patients who are treated in intensive care units or in the surgery department after surgery. This increasingly present complication complicates and calls into question the recovery of the operated patient. We assumed that POCD was associated with blood loss in patients undergoing colorectal cancer surgery.

Methods. Our study included 60 patients older than 50 years who underwent elective open surgery for colon cancer. The same protocol was performed for each patient: preoperative preparation and anesthesia. All patients completed three psychometric tests (mini mental test - MMT, information test and Hooper test) the day before surgery, one day after surgery and the seventh day after surgery.

Results. Cognitive status examined on the basis of the MMT score showed a statistically significant difference in the number of received blood transfusions after surgery on the first day ($p = 0.016$) and the total number of received blood transfusions ($p = 0.026$). Cognitive status examined by the information test showed a statistically significant difference ($p = 0.025$) in the number of received blood transfusions after surgery on the first day. In patients whose cognitive status was examined by the Hooper test, a high statistically significant difference was observed in the number of received blood transfusions after surgery on the first day ($p = 0.001$). Cognitive status measured on the basis of MMT score showed that there was a statistically significant difference in the average values of the amount of blood given by transfusion after surgery ($p = 0.019$).

Conclusion. There was a statistically significant cognitive dysfunction in patients who had greater blood loss during surgery and the first day after surgery and who received more blood transfusions (more than 600 ml) during and after surgery. The introduction of psychometric tests in the assessment of cognitive functions as well as the choice of surgery may be important factors in the prevention of POCD.

Key words: cognitive dysfunction, blood loss, psychometric tests, colorectal cancer

Introduction

Cognitive functions include complex brain functions such as general intellectual functions, attention, memory, comprehension, thinking, executive functions, planning, verbal functions, graphomotor functions, etc., which allow a person to acquire knowledge, analyze and assess events around themselves, and adequately response to various stimuli, problem solving and future planning [1]. Postoperative cognitive dysfunction (POCD) is a transient disorder, and yet a very significant complication that can occur after surgery, because memory impairment, ability to maintain concentration and information processing significantly affect the daily functioning of patients [2]. That is why it is very important to introduce psychometric tests for various cognitive functions in everyday work, which will enable easier detection, or recognition of cognitive dysfunction. Diagnosis requires preoperative and postoperative psychometric testing [3]. During extensive surgical interventions (resection of the colon) in the elderly, the probability of morbidity and mortality increases, and cognitive impairment has been reported very often [4, 5]. Observational studies have shown an association of postoperative hemoglobin concentration less than 10 g/L and an increased incidence of POCD [6, 7]. Some surgeries carry a higher risk of developing POCD than others, most often due to their complexity and large volume losses [8, 9]. Colorectal cancer is one of the most common cancers in modern man. Colon cancer is the third most common cancer in men, just behind lung and stomach cancer, and the third most common cancer in women, after breast and cervical cancer. It can occur at any age, but more than 90% of patients are older than 40 years, after which the risk doubles every ten years [10]. Surgery is the basic form of treatment for colorectal cancer, and the prognosis depends on the stage of the disease at the time of diagnosis. Between 80% and 90% of patients are cured if cancer is detected and treated at an early stage of cancer development. The aim of our study was to examine whether there is a relation between blood loss and POCD in colon cancer surgery.

Methods

Our study included 60 patients (35 men and 25 women) who underwent surgical resection of colon cancer, aged 50 to 84 years and educational level of 8 to 16 years of education. The diagnosis of the disease was made on the basis of a biopsy during a colonoscopy and histopathological findings. Patients were divided into two groups, depending on the type of anesthetic administered, group A - nesdonal (30 patients) and group B - propofol (30 patients), each other patient receiving the same anesthetic. Randomization was performed on the same principle. Every first subject received nesdonal and every second subject received propofol. The study included all patients who agreed to participate in the study and who signed an informative consent. Patients with stroke, psychiatric patients, patients with renal failure on dialysis and patients with severe systemic diseases were excluded from the study. Prior to inclusion in the study, each patient was diagnosed with cognitive status, i.e. the absence of severe cognitive dysfunction. We kept a separate card for each patient, designed only for this research. Upon admission to the hospital, we performed anesthesiological preparation of the patient for surgical treatment, which included anamnestic and physical examination of the patient, examination of medical documentation and decision on the type of anesthesia. We used the above standardized psychometric tests (mini mental test, information test and Hooper test) to verify and assess the state of cognitive functions in all patients. The state of cognitive functions was recorded immediately before the start of the surgery and after the first and seventh day after the completion of the surgery. All patients underwent the same anesthesia procedure at the secondary service level in the surgical operating room and intensive care unit. In premedication, patients received atropine 1 mg, midazolam 5 mg, and fentanyl 50 mcg I.M. (intramuscularly) half an hour before the start of surgery. Introduction to anesthesia was performed with nesdonal 5 mg/kg (group A) or propofol 2 mg/kg (group B) and leptosuccin 1.5 mg/kg. After intubation, anesthesia was maintained with fentanyl 5 mcg/kg, sevoran 0.2–5 minimum alveolar concentration (MAC) and pavulon (pancuronium bromide) 2 to 4 mg or tracrium (atracurium besilate) 0.3–0.6 mg/kg when needed muscle relaxation, in addition to sevoran as an inhalation anesthetic, air 1.5 L/min and O2 1.5 L/min were also included. At the beginning of the operation a central venous catheter was placed in the right internal jugular vein. All patients were monitored by prescribed standard monitoring (non-invasive measurement of arterial pressure, heart rate, saturation, ECG and central venous pressure). Half an hour before waking up each patient was administered a ketoprofen amp. 100 mg, metamizole sodium at a dose of 2.5 g I.V. (intravenous) and tramadol amp. 100 mg per infusion in the operating room. After the operation the patients were transferred to the ICU (intensive care unit) where they were connected to continuous monitoring of vital functions. Based on the value of CBC (complete blood count), and according to the obtained values (haemoglobin <100 g/L and haematocrit <0.25 L/L), transfusion of erythrocyte concentrate and FFP (fresh frozen plasma) was administered.

Results

All patients were divided into two age groups, one age group consisted of 32 patients, i.e. (53.3%), aged 50 to 68, and in the second age group there were 28 patients, aged 69 to 84, i.e. (47.7%). The average age of the patients was 68.51 ± 7.16. According to the gender structure, we had 35 men (58.3%) and 25 women (41.7%). Cognitive status examined on the basis of MMT score showed a statistically significant difference in the number of received blood transfusions after the operation on the first day (p = 0.016) and the total number of received blood transfusions (p = 0.026). Patients with cognitive impairment received significantly higher doses of blood transfusion after surgery on the first day (0.38 ± 0.49), and they had a higher number of total blood transfusions received (1.92 ± 1.23) compared to patients without cognitive impairment who received significantly fewer blood transfusions after surgery on the first day (0.11 ± 0.32) as well as the total number of blood transfusions received (1.16 ± 1.04). In the examined patients no statistically significant difference was observed in the number of administered blood transfusions during the operation and the number of received blood transfusions after the operation on the second day and more.

Table 1. Average values of the number of received blood transfusions during and after surgery of patients in relation to the cognitive status measured by MMT in patients after colon surgery

Received blood transfusions during and after surgery	Mini mental test (AS ± SD)		t	*p*
	Normal findings	Impairment of cognition		
Number of blood transfusions received during surgery	1.14 ± 0.71	0.38 ± 0.49	0.590	0.558
Number of blood transfusions received after surgery on the first day	**0.11 ± 0.32**	**0.38 ± 0.49**	**2.510**	**0.016**
Number of received blood transfusions after surgery on the second day and more	0.45 ± 0.80	0.16 ± 0.51	1.648	0.106
Total number of received blood transfusions	**1.16 ± 1.04**	**1.92 ± 1.23**	**2.285**	**0.026**

When the cognitive status of the patients (general intellectual ability) was examined by the information test a statistically significant difference (p = 0.025) was observed in the number of received blood transfusions after the operation on the first day. Patients who had below-average scores on the information test received a significantly higher number of blood transfusion on the first day (0,37 ± 0,48) compared to patients with above-average scores (0.11 ± 0.33). In the examined patients no statistically significant difference was observed in the number of received blood transfusions on the second day and more, as well as the total number of administered blood transfusions.

Patients whose cognitive status was examined on the basis of the Hooper test score showed a high statistically significant difference in the number of received blood transfusions after the first day of surgery (p = 0.001). Patients who were at high risk of cognitive impairment had a significantly higher number of administered blood transfusions after surgery on the first day (0.35 ± 0.48) compared to low-risk patients (0.11 ± 0.01). In the examined patients, no statistically significant difference was observed in the number of received blood transfusions during the operation, the number of received blood transfusions after the operation on the second day and more, as well as the total number of administered blood transfusions.

Table 2. Average values of the number of received blood transfusions during and after surgery of patients in relation to the cognitive status measured by the information test in patients after colon surgery

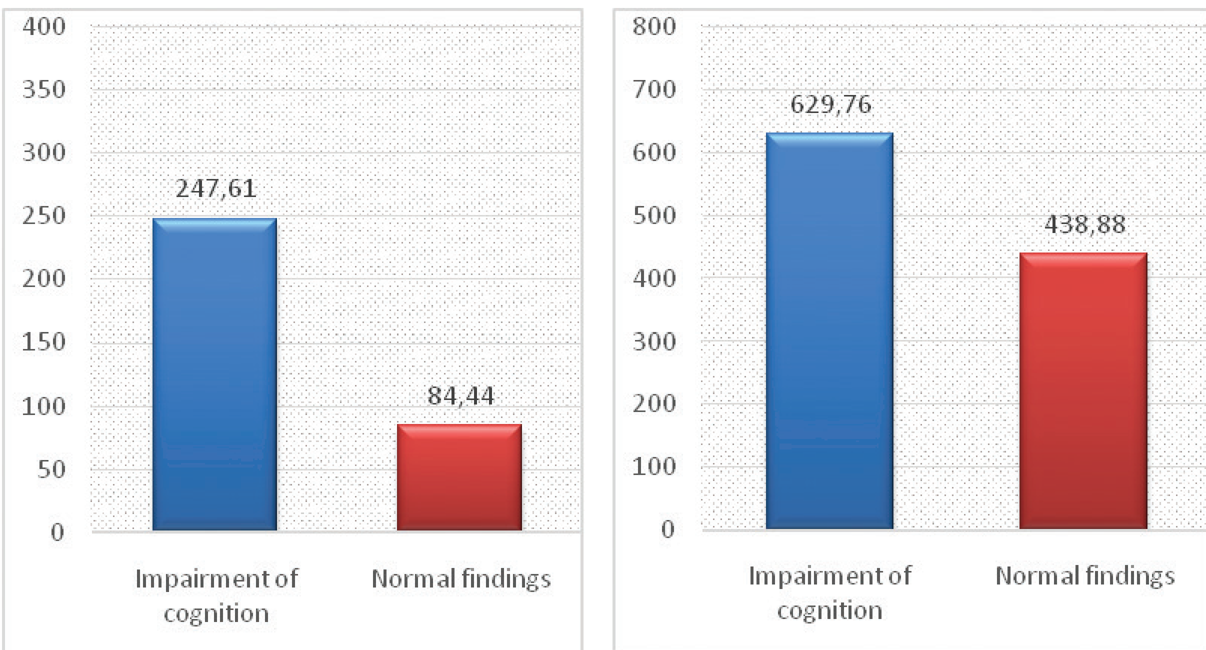
Received blood transfusions during and after surgery	Information test (AS ± SD)		t	*p*
	Above average	Below average		
Number of blood transfusions received during surgery	1.05 ± 0.74	1.13 ± 0.60	- 0.437	0.664
Number of blood transfusions received after surgery on the first day	**0.11 ± 0.33**	**0.37 ± 0.48**	**- 2.318**	**0.025**
Number of received blood transfusions after surgery on the second day and more	0.52 ± 0.71	0.30 ± 0.74	1.079	0.285
Total number of received blood transfusions	1.76 ± 0.90	1.67 ± 1.34	0.255	0.800

Table 3. Average values of the number of received blood transfusions during and after surgery of patients in relation to the cognitive status measured by the Hooper test in patients after colon surgery

Received blood transfusions during and after surgery	Hooper test (AS ± SD)		t	*p*
	Low risk	High risk		
Number of blood transfusions received during surgery	1.44 ± 0.52	1.05 ± 0.64	1.692	0.096
Number of blood transfusions received after surgery on the first day	**0.11 ± 0.01**	**0.35 ± 0.48**	**- 5.222**	**0.001**
Number of received blood transfusions after surgery on the second day and more	0.66 ± 0.86	0.31 ± 0.70	1.336	0.187
Total number of received blood transfusions	1.77 ± 0.66	1.68 ± 1.30	0.205	0.838

When cognitive status was measured based on the MMT score a statistically significant difference was observed in the average values of the amount of blood given by transfusion after surgery (p = 0.019). Patients who had impaired cognition on MMT received a significantly higher amount of blood (247.61 ± 260.31 ml) after surgery compared to patients with normal findings (84.44 ± 225.52 ml). There was a statistically significant difference between the mentioned groups of patients in the average values of the total amount of blood given during and after the surgery, whereby patients with impaired cognition received significantly more blood during and after the surgery (629.76 ± 374.89 ml) in relation to patients without cognitive impairment (438.88 ± 297.02 ml).

Analysis of risk factors for cognitive impairment after anesthesia in colon cancer surgery revealed that a higher number of transfusions was given during surgery (OR = 1.597, [Cl = 1.098-5.951], p < 0.001) and a larger amount of blood was given during surgery (OR = 1,938, [Cl = 2,704-7,298], p < 0.001) represent statistically significant risk factors for the occurrence of cognitive impairment after colon cancer surgery. These factors are associated with a high risk of deteriorating cognitive function in these patients. The mean value of Hgb after surgery was 116.08 ± 19.59 g/L, and mean value of Hct after surgery was 0.34 ± 0.05 L/L. The significant difference between mean values of Hgb and Hct between groups of patients divided by number of administered transfusions on the first and second day after surgery was not observed (Figure 1).



Total amount of blood given after surgery

Total amount of blood given during and after surgery

Figure 1. Cognitive status after surgery - MMT

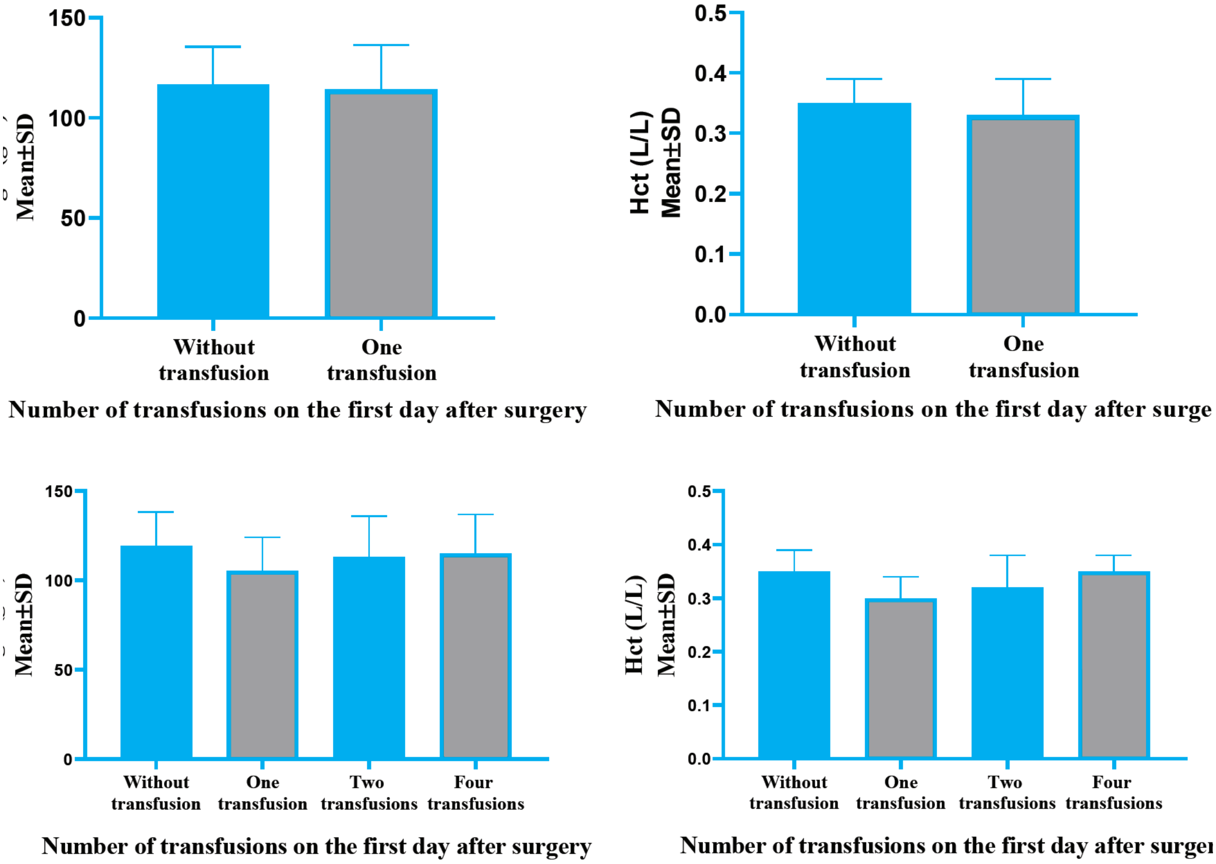


Figure 2. Mean concentrations of Hgb and Hct between groups of patients devided by number of administered transfusions on the first and second day after surgery

Hgb - haemoglobin, Hct - haematocrit; SD - standard deviation: ANOVA - univariate analyses of variance

Discussion

Blood viscosity affects cerebral blood flow and the value of haematocrit is the primary cause of viscosity. The decrease in haemoglobin due to dilution reduces the arterial oxygen content, so if there is no simultaneous increase in cerebral flow, there is a drop in oxygen supply. During colon surgery due to blood loss it comes to the hemodilution, so that blood flow through the brain and blood consumption in the brain fall at the same time. It is difficult to determine optimal haematocrit that will maintain normal oxygen supply, but also optimal blood flow through the brain, because it is involved in complex interaction with other parameters (temperature, depth of anaesthesia, etc.) that affect blood flow through the brain [11]. Nevertheless, some larger studies have found a trend towards increased morbidity and mortality in haematocrits lower than 22% [12, 13, 14]. It has been found that the lowest measured haematocrit value of 10% can be an independent stroke factor, and the risk increases for each percentage point of haematocrit decline [15]. Significant hemodilution (haematocrit between 15% and 17%) was related to a higher incidence of cognitive impairment six weeks after surgery [16]. In circumstances of excessive hemodilution, blood transfusion, to increase haematocrit, carries a new risk. Namely, studies that found that a haematocrit lower than 22% causes an increase in cognitive impairment also showed that transfusion, with the aim of reversing the negative impact of hemodilution, can have an adverse effect on renal function and cause their stagnation. Therefore, it is safest to apply all methods to avoid excessive hemodilution during major surgical interventions. Due to the importance of prevention of cerebral ischemia, intraoperative monitoring of haematocrit levels, blood oxygen saturation (pulse oximetry) and monitoring of the operative field (volume of bleeding) are necessary [17]. Our results unambiguously show that a larger number of transfusions (more than two doses) as well as a larger amount of blood (more than 600 ml) administered during and the first day after surgery affect POCD. The methods currently available that identify cognitive impairment are neither specific nor sensitive enough. Current guidelines suggest the use of combined tests to improve the accuracy of predicting the occurrence of cognitive deficits. There is still a search for simple and effective methods, tests for early detection of mild cognitive changes, which is necessary for their more efficient treatment and prevention. Patients with severe cognitive impairment are usually excluded from the study and this results in the selection of subsamples of cognitively less impaired patients [18, 19]. Also, it should be taken into account that MMT is a neurocognitive instrument for measuring the global cognitive level with strict sensitivity to language deficit. The information test is a test of conceptual thinking and is a measure of general intellectual ability. This test is one of the most resistant tests to brain decline, so it can be used as a rough measure of premorbid intelligence. The Hooper test is the most well-known test of visual organization and is sensitive to the detection of brain pathology, as well as the detection of fragmentary perception. Postoperative cognitive impairment is defined as worsening of results in one or more tests. Based on these tests, we determined for each of the patients whether or not he had a cognitive disorder.

Conclusion

There was a statistically significant cognitive impairment in patients who had greater blood loss during surgery and the first day after surgery and received more blood transfusions (more than 600 ml) during and after surgery. The introduction of psychometric tests in the assessment of cognitive functions as well as the choice of surgery may be important factors in the prevention of POCD.

Funding source. The authors received no specific funding for this work.

Ethical approval. The Ethics Committee of the Hospital "Serbia", East Sarajevo, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

References:

1. Cao SJ, Chen D, Yang L, Zhu T. Effects of an abnormal mini-mental state examination score on postoperative outcomes in geriatric surgical patients: a meta-analysis. BMC Anesthesiol 2019;19(1):74.
2. Evered LA, Silbert BS. Postoperative Cognitive Dysfunction and Noncardiac Surgery. Anesth Analg 2018;127(2):496–505.
3. de Boer C, Mattace-Raso F, van der Steen J, Pel JJM. Mini-Mental State Examination subscores indicate visuomotor deficits in Alzheimer's disease patients: A cross-sectional study in a Dutch population. Geriatr Gerontol Int 2014;14(4):880–5.
4. Huang C, Mårtensson J, Gögenur I, Asghar MS. Exploring Postoperative Cognitive Dysfunction and Delirium in Noncardiac Surgery Using MRI: A Systematic Review. Neural Plast 2018;2018:1281657.
5. Zhang J, Liu G, Zhang F, Fang H, Zhang D, Liu S, et al. Analysis of postoperative cognitive dysfunction and influencing factors of dexmedetomidine anesthesia in elderly patients with colorectal cancer. Oncol Lett 2019;18(3):3058–64.
6. Williams GA, Hudson DL, Whisenhunt BL, Stone M, Heinberg LJ, Crowther JH. Short-term changes in affective, behavioral, and cognitive components of body image after bariatric surgery. Surg Obes Relat Dis 2018;14(4):521–6.
7. Zhu SH, Ji MH, Gao DP, Li WY, Yang JJ. Association between perioperative blood transfusion and early postoperative cognitive dysfunction in aged patients following total hip replacement surgery. Ups J Med Sci 2014;119(3):262–7.
8. Saindane AM, Drane DL, Singh A, Wu J, Qiu D. Neuroimaging correlates of cognitive changes after bariatric surgery. Surg Obes Relat Dis 2020;16(1):119–27.
9. Sharma N, Wig J, Mahajan S, Chauhan R, Mohanty M, Bhagat H. Comparison of postoperative cognitive dysfunction with the use of propofol versus desflurane in patients undergoing surgery for clipping of aneurysm after subarachnoid hemorrhage. Surg Neurol Int 2020;11:174.
10. Blacher RS. On awekening paralyzed during surgery:A syndrome of traumatic neurosis. JAMA 1975;234(1):67–8.
11. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the Nomenclature of Cognitive Change Associated with Anaesthesia and Surgery-2018. Nomenclature Consensus Working Group. Anesthesiology 2018;129(5):872–9.
12. Yuan SM, Lin H. Postoperative Cognitive Dysfunction after Coronary Artery Bypass Grafting. Braz J Cardiovasc Surg 2019;34(1):76–84.
13. Wan J, Luo P, Du X, Yan H. Preoperative red cell distribution width predicts postoperative cognitive dysfunction after coronary artery bypass grafting. Biosci Rep 2020;40(4):BSR20194448.
14. Ranucci M, Biagioli B, Scolletta S, Grillone G, Cazzaniga A, Cattabriga I, et al. Lowest haematocrit in cardiopulmonary bypass impairs the outcome in coronary surgery. Tex Heart Inst J 2006;33(3):300–5.
15. Karkouti K, Djaiani G, Borger MA, Beattie WS, Fedorko L, Wijeysundera D, et al. Low hematocrit during cardiopulmonary bypass is associated with increased risk of perioperative stroke in cardiac surgery. Ann Thorac Surg 2005;80(4):1381–7.
16. Lin X, Chen Y, Zhang P, Chen G, Zhou Y, Yu X. The potential mechanism of postoperative cognitive dysfunction in older people. Exp Gerontol 2020;130:110791.
17. Tan CB, Ng J, Jeganathan R, Kawai F, Pan CX, Pollock S, et al. Cognitive changes after surgery in the elderly: does minimally invasive surgery influence the incidence of postoperative cognitive changes compared to open colon surgery? Dement Geriatr Cogn Disord 2015;39(3-4):125–31.
18. Rubin DS, Peden CJ. Preoperative Frailty and Cognitive Dysfunction Assessment. Anesthesiol 2020;133(6):1164–6.
19. Belrose JC, Noppens RR. Anesthesiology and cognitive impairment: a narrative review of current clinical literature. BMC Anesthesiol 2019;19(1):241.

Uticaj perioperativnog gubitka krvi na poremećaj kognitivnih funkcija poslije operacije karcinoma debelog crijeva

Dalibor P. Bošković[1], Sanja S. Marić[2], Marko B. Kovačević[1], Bojan R. Golijanin[1]

[1]JZU Bolnica "Srbija" Istočno Sarajevo, Republika Srpska, Bosna i Hercegovina

[2]Univerzitetska bolnica Foča, Republika Srpska, Bosna i Hercegovina

Uvod. Postoperativni kognitivni deficit (POKD) se veoma često javlja kod bolesnika koji se poslije operacije liječe u jedinicama intenzivne njege ili na odjeljenju hirurgije. Ova sve češće prisutna komplikacija otežava i dovodi u pitanje oporavak operisanog pacijenta. Pretpostavili smo da je POKD povezan sa gubitkom krvi kod pacijenata koji su podvrgnuti operaciji kolorektalnog karcinoma.

Metode. U naš rad je bilo uključeno 60 pacijenata starijih od 50 godina koji su bili podvrgnuti elektivnoj otvorenoj operaciji karcinoma debelog crijeva. Za svakog pacijenta je bio sproveden isti protokol - preoperativna priprema i anestezija. Svi pacijenti su ispunili tri psihometrijska testa (mini mental test – MMT, test informisanosti i Huperov test) dan prije operacije, jedan dan poslije operacije i sedmog dana poslije operacije.

Rezultati. Kognitivni status ispitivan na osnovu skora MMT pokazao je statistički značajnu razliku u broju primljenih transfuzija krvi nakon operacije prvog dana ($p = 0,016$) i ukupnog broja primljenih transfuzija krvi ($p = 0,026$). Kognitivni status ispitivan testom informisanosti pokazao je statistički značajnu razliku ($p = 0,025$) u broju primljenih transfuzija krvi nakon operacije prvog dana. Kod pacijenata čiji je kognitivni status ispitivan Huperovim testom uočena je visoka statistički značajna razlika u broju primljenih transfuzija krvi nakon operacije prvog dana ($p = 0,001$). Kognitivni status izmjeren na osnovu skora MMT pokazao je da postoji statistički značajna razlika u prosječnim vrijednostima količine krvi date transfuzijom poslije operacije ($p = 0,019$).

Zaključak. Prisutan je statistički značajan poremećaj kognitivnih funkcija kod pacijenata koji su tokom operacije i prvog dana poslije operacije imali veći gubitak krvi i dobili veći broj transfuzija krvi (više od 600 ml) tokom i poslije operacije. Uvođenje psihometrijskih testova u procjenu kognitivnih funkcija, kao i izbor hirurške operacije mogu biti značajni faktori u prevenciji POKD.

Ključne riječi: kognitivni deficit, gubitak krvi, psihometrijski testovi, kolorektalni karcinom