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Postoperative cognitive dysfunction: physiopathological aspects and clinical evidence

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Abstract

Background: Postoperative cognitive dysfunction (POCD) represents a decrease of cognitive abilities (memory, learning, concentration), which develops in the postoperative period after a variable amount of time (days or weeks). Today, the pathogenesis of the POCD development is not fully known. Literature suggests multiple possible mechanisms of POCD development. Certainly, the neuro-inflammatory effect (generated by the surgery itself) from the cortical zones responsible for learning and memory, is one of the phenomena frequently noted in these patients. This article is a narrative synthesis of literature on postoperative cognitive dysfunction – a quite spread phenomenon found in patients during postoperative care. We described suggested theories and the pathophysiological mechanisms involved in the development of this clinical condition. Its incidence according to different types of surgery is presented. We reviewed the available tools for identification and qualitative assessment of postoperative cognitive dysfunction, including biomarkers. Also, we discuss the risk factors for postoperative cognitive dysfunction and their role in clinical decision making process.
Conclusions: Postoperative cognitive dysfunction is a common complication after the surgery. It occurs in frail patients or in individuals presenting general risk factors. It looks like there is a genetic predisposition for the development of postoperative cognitive dysfunction. Patients at risk of postoperative cognitive dysfunction can be identified by neurocognitive testing tools.
Key words: postoperative cognitive dysfunction, risk factors, biochemical markers.

Introduction

Postoperative cognitive dysfunction (POCD) represents a decrease of cognitive abilities (memory, learning, concentration), which develops in the postoperative period after a variable amount of time (days or weeks).

Today, the pathogenesis of the POCD development is not fully known. Literature suggests multiple possible mechanisms of POCD development. Certainly, the neuro-inflammatory effect (generated by the surgery itself) from the cortical zones responsible for learning and memory, is one of the phenomena frequently noted in these patients [1]. Among POCD risk factors we find: age, intraoperative hypoxemia, intensity of pain in the perioperative period, extent and length of surgery, number of surgical interventions, postoperative complications (infectious, respiratory, stroke) etc [2, 3].

POCD causes a decrease in quality of life and enhances 1 year mortality [4]. POCD incidence is reported to be between 24 and 79% (short term) and 57% (long term) [5].

Neuroinflammatory theory

Riedel B. et al. [6] comes with a recent data analysis in order to understand physiopathology of POCD. So, POCD is a well-known syndrome, present in approximately 15% of patients of 60 years and older, characterized by a decrease of cognitive function as a consequence of anesthesia and surgery. Recent data suggests that POCD is mediated by the neuro-inflammatory response that is strongly related to the surgical intervention. Questions arise regarding the casualty of the inflammatory process, endothelial dysfunction and POCD.

Systemic inflammatory response, in combination with endocrinological, metabolic and immunological modifications plays an essential role in recovery and wound healing. Even though, all recent studies show that the inflammatory status is associated with negative perioperative results. Therefore, interventions that modulate the inflammatory response, surgery, anesthesia and drugs may enhance the recovery and reduce complications. Research about wound physiology underline the importance of genetic variability in systemic inflammatory response [7]. Zhu J. et al. [8] published a study where he finds links between appearances of cognitive dysfunction following cardiac ischemia. The study was performed on animal model, where direct implication of the neuroinflammatory step in POCD is shown.

Theory about mediators disbalance

Recent studies tend to prove the relationship between POCD and disbalance of mediators. Cytokines that are activated by various factors during surgery are capable of affecting memory operational system. Interleukin IL-1β is one of the most important mediators that leads to inflammatory response in the brain. IL-1β has local effects that depend on concentration and act on the hippocampus and memory.

Lipopolysaccharides, one of the components of the external membrane of gram negative bacteria are a strong trigger of inflammatory response. Confirmation of this data can be found in publications of Fidalgo A. et al. [9].

Anti-inflammatory cholinergic pathway is a neurohumoral mechanism that plays an important role in inflammatory response suppression. Usage of cholinesterase inhibitors

raises cholinergic transmission, thus, may act as a potential approach for prevention of neuroinflammation. Kalb A. et al. [10] uses an animal model to reach results that state: intraoperative administration of cholinesterase inhibitors leads to a decrease in the pro-inflammatory response and lowers neurodegeneration in the cortex and hippocampus. This combination may represent an instrument in pathogenesis of POCD.

Genetics' theory

Apolipoprotein E (APOE) is a lipoprotein with small molecular weight, synthesized predominantly in the liver. Its role is to control cholesterol metabolism. Three types of APOE exist: E2, E3, E4; being encoded as alleles: e2, e3, e4 according to Gerdes L. et al. [11]. Allele e4 is the one that correlates with atherosclerosis and Alzheimer. People having this allele have difficult rehabilitation after cerebral injury. Tardiff B. et al. [12] performs a study which included 65 patients after cardiac surgery, analyzing plasmatic concentration of APOE, especially allele e$, evaluates preoperative data about neuropsychological tests, age and educational level, and concludes that there is an important association between APOE e4 and POCD at 6 weeks distance after cardiac surgery. In 2007, Olney J. et al. [13] affirms that APOE allele e4 is the factor which predisposes to late postoperative delirium. Controversial results are brought by Abildstrom H. et al. [14] in a study performed on 976 patients of the same age (40 years old) that underwent non-cardiac surgery. The conclusion states that POCD is not associa-ted with APOE allele e4. The same conclusions are reached by McDonagh D. et al. [15] that affirms that patients with APOE genotype do not correlate with POCD in non-car-diac surgery. Mathew J. et al. [16] creates a hypothesis which states that POCD is genetically drived as a result of genetic polymorphism of biological inflammatory regulation, cellular adhesion, coagulation, fat metabolism and vascular reactivity. Authors aim to monitor 37 unique nucleotides associated with cognitive decrease at 6 weeks after the surgery. Genetical variations of C-reactive protein and P-selectine were implied in the cognitive decrease after cardiac surgery. As a consequence of these genetic variations, patients can be placed in risk groups, and it could be useful as a perioperative anti-inflammatory strategy.

If physiopathological mechanisms of POCD are open for new research, then the clinical aspects, through the prism of evidence based medicine, seem to offer a much larger picture.

POCD in cardiac and vascular surgery

First researches made in order to prove POCD were made in cardiac surgery. Cerebral complications are frequent in cardiac surgery. Incidence of POCD in cardiac surgery varies between 30 and 80% during the first postoperative week and around 60% after several months, Rasmussen L. et al. [17]. A recent study performed by Toeg H. et al. [18], confirms the presence of POCD in 38% of cases at discharge and 19% at 3 months after the surgery. Tournay-Jette E. et al. [19] published results that cognitive dysfunction that appears after cardiac surgery has an incidence of 80.7% in elderly population. POCD was documented after different types of surgery. Evered L. et al. [20] performs a study where he compares different types of surgeries, which were followed by POCD. Evered L. includes patients that underwent coronary angiography with sedation, total hip replacement and coronary by-pass under general anesthesia. It was noticed on postoperative day 7, POCD is more frequently seen in patients after coronary by-pass, and after 3 months no differences were found between the study groups. Newman M. et al. [21] concludes that ¾ of patients that underwent coronary by-pass, suffer from neurocognitive dysfunction at discharge, and about 1/3 of patients – at 6 months distance from the surgery. Thus, Newman M. performed another study on patients after 5 years from the surgery to evaluate POCD in long term. POCD incidence at 5 years after the surgery was almost the same as POCD incidence at discharge. POCD at discharge is predictive for its long term presence as well. This justifies the early POCD treatment. A similar study was made by Knipp S. et al. [22] with similar results.

Dijk D. et al. [23] as well studied POCD in patients after coronary by-pass surgery at 5 years distance. Many authors attributed cognitive decline to age modifications rather than a surgical event. This theory was sustained by Selnes O. et al. [24]. Controversial results are brought by Rosengart T. et al. [25] which performed a study on patients that were about to have surgery for coronary by-pass. No differences were found between control and study group. This difference between other studies and the study of Rosengart T. was explained by different evaluation methodologies and statistical analysis. The same affirmations we find in the study of Sweet J. et al. [26]. POCD was not confirmed after coronary by-pass surgeries.

POCD in non-cardiac surgery (minor and major)

Researches from modern medicine evaluated patients with non-cardiac pathologies. Such studies were performed in 1998 by the research group ISPOCD1 which evaluated patients that underwent a major non-cardiac surgery, pro-ving that 26% of patients suffer from POCD at 1 week distance and about 10% – at 3 months distance. Monk T. et al. [2] also proves POCD in patients that underwent major non-cardiac surgery and has a significant impact on 1 year mortality. Newman S. et al. [27] affirms that POCD during the first weeks after cardiac surgery is significant and its percentage increases with age. POCD at 6 months distance is very low and could be occasionally present in particular cases. POCD in major non-cardiac surgery was studied by Dijkstra J. et al. [28]. POCD was found in the first postope-rative week. At 3 months distance, patients had good results, cases of cognitive changes are particular, and do not reflect the surgical factor, but other factors such as depression and age.

POCD in elderly patients (minor and major surgery)

For the first time, POCD in elderly patients was described by Bedford in 1955 [29]. In such a way, Bedford starts a new trend of demonstrating, proving and researching a new branch of pathologies that interferes with surgery and anesthesia. One of the biggest studies is the ISPOCD1, made by Moller et al. [30] which confirms appearance of long term POCD in elderly patients. Major surgery is frequently associated with POCD in elderly patients. POCD after minor surgery is found in publications of Canet J. et al. [31]. POCD incidence in elderly patients after minor surgeries reaches

9.7%. Comparing with previous studies of Canet J. in minor and major surgery, it is stated that incidence of POCD in minor surgery in elderly is lower.

MRI is used in monitoring of Alzheimer starting with pre-symptomatic phases in order to predict earlier the symptomatic phase. Kline R. et al [32], based on MRI data of patients with Alzheimer, fried to demonstrate the hypothesis that surgery might have an impact on the brain structures with progression of dementia postoperatively. The study included elderly patients. The obtained results showed that in patients that underwent surgery, in the first 5-9 months after the surgery (but no later), rates of gray matter atrophy increased in the cortex, hippocampus and lateral ventricle extended, comparing with the control group (non surgical). Neuro-psychological tests applied to these patients elucidated cognitive decrease in patients from the surgical group. Thus, elderly patients that underwent surgery had higher rates of cerebra atrophy and an increased risk of POCD. On the other hand, no correlation has been found between cerebral atrophy and patients that had mild cognitive dysfunction in the immediate postoperative period and with significant results of cognitive dysfunction later.

POCD in middle-aged patients (minor and major surgery)

POCD in patients of middle age in non-cardiac surgery has been studied by Johnson T. et al. [33] in 2002. POCD after non-cardiac surgery is associated with age, on the other hand, patients of middle age have a lower incidence. Thus, the research hypothesis appeared, and the researches analyzed 463 patients at 1 week postoperatively, and found that 19.2% suffer from POCD. At 3 months distance, POCD has decreased to 6.2%. As mentioned before, Abildstrom H. et al. [14] studies POCD in patients of middle age and has stated an incidence of 11.7% of POCD.

POCD in young patients (minor and major surgery)

Monk T. et al. published data about POCD in young patients in 2008 [2]. The study aimed at identifying POCD in non-cardiac surgery, where patients of all ages are included. Authors were able to prove that POCD was found to be equal in young patients, middle age and elderly. Fact which contradicts the ISPOCD1 study. Monk T. also affirms that recovery at 3 and 12 months after the surgery is better in young patients.

POCD in pregnant (minor and major surgery)

Minor and major surgical procedures are associated with cognitive changes: memory loss and lack of concentration. If this is not diagnosed and treated promptly, this pathology may lead to serious consequences. The author supposes that POCD may appear as well after obstetrical interventions such as C-section and natural delivery, influencing the mother or the baby. Obstetrical or neonatal POCD is now fully known. The majority of studies performed focused on the risk factors such as: type of anesthesia, medication, intervention, stress etc. C-sections and obstetrical anesthesia are being used more frequently nowadays, and we can affirm that POCD will be found in this group of patients as well. Thus, maternal and child brain is subject of an increased risk of cognitive decrease with serious consequences. In conclusion, we can cite S. Ghosh [34]: "*Real nature and incidence of POCD is complex and remains to be explored as its existence in obstetrical anesthesia cannot be excluded*".

Predictive and risk factors for POCD

Predictive and risk factors for POCD are not well established, but the recent studies try to clarify this problem. POCD seems to be a multifactorial. These factors can be divided into pre, intra and postoperative.

a) Preoperative factors – are factors that were present before surgery (genetic, APOE allele e4 theory, C-reactive protein and P-selectine).

Demographic factors (age and educational level). Age is one of the most controverted factors, cognitive decline is inevitable with age and it is difficult to draw conclusions on this matter (where exactly we have normal cognitive function and where we have a pathological decline due to hospitalization). Regarding educational level: patients with a higher educational level have a lower incidence of POCD.

Obtained risk factors during life time: general medical conditions, pain-killers, a specific disease (such as hypertension), POCD established before sugery, substance abuse, etc.

b) Intraoperative factors or *stressing factors* are those which start on the day of the surgical intervention. This group contains the surgery itself, anesthesia, used pain-killes, hypoxia and intraoperative hypotension etc.

c) Postoperative factors are those factors that encouraged and maintained POCD: sedation, analgetics in the postoperative period, infections etc [35]), (tab. 1).

Methods of quantification and evaluation of POCD

Psychrometric tests

Appreciation of postoperative cognitive decline was made through a large variety of methods; large number of types of surgical interventions and the big variety of psychological tests make standardization difficult. Cognitive performance of each individual is different, due to educational level, neuronal reserve, factors that influence each patient during examination (tiredness, insomnia, stress etc). The majority of authors agree that cognitive performance of the patient should be compared only with the performance of the same patient.

Ghoneim M. et al. [47] considers that POCD may be diagnosed using only neuro-psychological tests. Neuro-psychological tests have the goal to identify and quantify cognitive abilities. They are designed to evaluate different domains of cognition such as: general intellectual function, memory, attention, concentration, speed of processing and executive function. There are several tests in each domain. Test selection aims to identify even minor changes, it is difficult to achieve high scores at these tests. This kind of tests is used for patients with high intellectual level that have high scores at initial testing. Sometimes it is necessary to use low-score tests for specific patients. Ghoneim M. suggests using several, most popular, tests for POCD appreciation. *"Digit Span"* and *"Wechsler Adult Intelligence Scale – Revised Test"* are oriented to test working memory. *"Digit Symbol Substitution"* characterizes speed of processing of information and working memory. *"Rey Auditory Verbal Learning Test"* has the goal to teach verbally, revoke and reproduce. *"The Stroop*

Table 1

Risk factors for POCD

Reference	Risk factors and comments
	Genetic factors and specific enzymes
Tardiff B et al. 1997 [12]	Apolipoprotein allele E4
Mathew J et al. 2007 [16]	C-reactive and P-selectine
Gaudet J et al. 2010 [36]	MMP 9 (matrix metalloproteinase)
Rasmussen L et al.1999 [37] Moller J et al. 1998 [30] Johnson T et al. 2002 [33] Monk T et al. 2008 [2] Moritz S et al. 2008 [38] Carrascal Y. 2005 [39] Sanders RD et al. 2010 [40]	Advanced age Patients older than 60 have a significant risk of long-term cognitive dysfunctions Increased mortality during the first postoperative year
Monk T et al. 2008 [2] Sanders RD et al. 2010 [40]	Educational level
Johnson T et al. 2002 [33]	Alcohol abuse. Interferes with effects of premedication and could lead to POCD in the immediate postoperative period
Bodolea C. 2010 [35]	POCD present before admission
Monk T et al. 2008 [2] Sanders RD et al. 2010 [40]	Stroke
Bodolea C. 2010 [35]	Arterial hypertension
Monk T et al. 2008 [2]	POCD at discharge is a risk factor for cognitive decrease at 3 months postoperatively
	Surgery
Sanders RD et al. 2010 [40]	Major surgery and history of surgeries in the past
Carrascal Y et al. 2005 [39] Evered L et al. 2011 [20]	Cardiac and valvular surgeries
Olney JW et al. 2000 [13] Culley DJ et al. 2007 [41] Kavanagh T et al. 2012 [42] Sanders RD et al. 2010 [40]	Type of anesthesia
Moller J et al. 1998 [30] Browne S et al. 2003 [43] Sanders RD, et al. 2010 [40] Saricaoglu F et al. [44]	Hypoxia and hypotension during surgery
Sanders RD et al. 2010 [40] Stanley T et al. 2002 [45]	Atrial fibrillation
Leiendecker J et al. 2010 [46]	Migrant micro-embolism during surgical interventions
Sanders RD et al. 2010 [40]	Infections and postoperative complications in the past

Test" evaluates attention, concentration and executory function. *"Grooved Peg Board"* – manual dexterity and psychomotor coordination. "The Trail Making Test" – attention, mental flexibility and motor function. Also, it is recommended to test anxiety and depression, as these factors may lead to lower performance during testing. Anxiety is usually tested with *"State Trait Anxiety Inventory"*. Depression is usually tested with *"The Beck Depression Inventory"* and *"Center for Epidemiological Studies Depression Scale"*.

Carrascal Y. et al. [39] proposes a single test for POCD appreciation. He performs a study, enrolling 132 patients and uses *"Paced Auditory Serial Addition Test"*. Authors conclude that the percentage of POCD after cardiac surgery was equal to results of studies made using several tests. These tests are easy to use, they can be reproduced and they represent a simple and practical method of POCD testing after cardiac surgeries.

A Swedish study made by Jildenstal P. et al. [48] studies the evoked auditory potential during ophthalmological surgeries. Peculiarities of ophthalmologic surgeries limit application of a large spectrum of neuro-psychological tests; nevertheless, authors prove the utility of auditory evoked potential.

How neuro-psychological tests are applied

An important role in POCD appreciation is played by the fact how the tests are applied, the timing, number of evaluations, number of tests used etc. Rasmussen et al. [17] comes with several recommendations regarding the design of such studies. We will discuss these aspects.

Selection and application of tests

a) Objective vs. subjective tests. Neuropsychological tests should detect even small cognitive changes by evaluating several intellectual and personal aspects. One can use MCQ-blank, pencil-paper or various computed applications. Usually these tests require time and effort but can contain subjective complaints from patients. These tests are highly dependent on patients' expectancies, self-respect and should not be implied for POCD evaluation.

b)Variability. Neuropsychological tests should be the same in both testing sessions, under the same circumstances, at the same time of the day. External exciting factors should be minimized, drugs that impede cognitive function should also be discontinued (opioids, hypnotics), also testing should not be performed if patient is in pain.

c) *Basal Performance.* Basal, preoperative, normal levels should be evaluated if patients experience tiredness, anxiety and depression while hospitalized. Rasmussen recommends primary evaluation to be done 1-2 weeks before surgery.

d) Exercising effect. Using the same set of tests favours memorizing. This way, performance is artificially improved. In order to exclude that, it is recommended to use parallel forms of these tests, re-testing with longer intervals of time or using a control group.

e) Intervals between testing. Time intervals between testing depend on specific clinical situations. Tests are applied upon discharge or at the first postoperative control. Demotivation and tiredness may lead to subestimation and lower levels of cognitive performances, than can easily be confounded with demotivation and chronic tiredness. If patients are not tested because of pre-existent cognitive dysfunction, the impossibility of testing may hide patients with cognitive decline and subestimate obtained data.

f) Emotional modifications and anxiety. Depression and anxiety lead to lower cognitive performances. Rasmussen recommends questionnaires that evaluate these variables.

g) Drop-out. Drop-out means losing patients during the study. Patients abandon the study due to lack of interest, lack of time at discharge and even because of POCD itself. It is recommended to report drop-out, this way; these patients may be attributed to POCD.

Rasmussen et al. [17] recommends basic criteria of test selection:

1) *Linguistic and cultural issues.* Most of the tests are written in English. Translating and adapting tests requires careful analysis and word selection according to local culture and using control groups. Patients with low intellectual levels may have difficulties in understanding some words.

2) *Parallel versions.* Parallel versions that are used in order to exclude familiarization with the test may induce a cognitive decline that is improperly calculated by a non-equivalent form of testing.

3) *Sensibility.* Tests with low sensibility, such as "*Wechsler Adult Intelligence Scale*" or "*Wechsler Memory Scale*" are frequently used for POCD evaluation but do not identify fine cognitive dysfunction.

4) *Inferior and superior limit effect.* Neuro-psychological tests that are difficult to achieve a minimal score, or, vice-versa, tests that are very easy in obtaining the highest score lead to subestimation of obtained data.

5) *Time and errors.* It is preferably to use tests that can count the number of errors, and in case of no mistakes – that can take into consideration the total time of testing.

Nevertheless, POCD evaluation requires a set of tests in order to be able to appreciate a larger spectrum of cognitive functions. But it is important to have in mind the time required to perform the testing. Testing should not make the patient tired, because this will lead to incorrect data. Some authors recommend calculation of performances from all tests in a single score. This may cause another difficulty, allowing some researchers to lower or increase the proportion of POCD, Bodolea C. [35].

Biochemical markers

POCD is currently diagnosed with neuropsychological tests, this method being the main assessment tool.

Variability and difficulty in applying neuropsychological tests led researchers to look for POCD-specific biochemical markers. Determination of specific markers will allow the tracking of the evolution and the prevention of this pathology. Thus, Rasmussen et al. [17], analyses the action of neuron-specific enolase (NSE) and S-100b protein, both of which are early markers in cerebral injuries. Obvious correlations have been observed in S-100b plasma levels in abdominal surgery and postoperative delirium patients. There was no correlation between POCD and blood concentrations of NSE and S-100β protein in abdominal surgery. While in cardiac surgery, namely coronary bypass, the authors had a significant increase in both biomarkers at 24 and 48 hours. Except that NSE in the statistical analysis correlates with POCD having a significant increase at 24 hours postoperatively. While the increased plasma concentration of the S-100b protein correlates with the duration of surgery. So NSE seems to be a blood marker for early POCD after coronary bypass.

The role of biomarkers in the DCPO predictor such as the S-100β protein and the anticholinergic active serum (AAS) was evaluated by Plaschke K. et al. [49]. This hypothesis is put by Plaschke on the grounds that AAS has previously been described as a risk factor in the appearance of the delirium to elderly patients. In contrast to the increased intraoperative plasma concentration of S-100β protein, the association of AAS with POCD was not detected. Nitric oxide is a powerful vasodilator. In the central nervous system, nitric oxide functions as a neurotransmitter. The increase in the concentration of nitric oxide and its products, nitrites and nitrates, was observed by Molnar T. et al. [51] in his paper he aims to evaluate the link between PODC and the biomarkers of immuno-endothelial dysfunction, which may be linked to ischemia and neurocognitive changes in pulmonary onco-surgery. Thus, it analyzes a series of biomarkers such as soluble P-selectin, soluble ligand, CD40 as the biomarker of platelet activation, soluble vascular cell adhesion molecule-1, MCP-1 (monocyte chemoattractant protein-1) Interleukins IL-6, IL-8, C-reactive protein and S100B protein. Therefore, the platelet and endothelial-related molecules had a preoperative plasma concentration and 48 hours postoperatively plasma concentration in patients who

developed POCD. Significant increase at 48-hour postoperative was notes for values of MCP-1 and S100B-protein. The authors assume that the endothelium and thrombocytes are activated as a response to the immune system and the presence of tumor agents. Translocation of leukocytes with deterioration of the blood-brain barrier and brain ischemia with the appearance of POCD occurs after the preoperative activation of endothelium and platelets. Following the increase of these preoperative markers, patients in the risk group who may develop POCD could be identified and it is possible to even modify therapeutic course, and why not, avoid surgical intervention in case of risk of the major neurocognitive injury of oncological patients.

In 2010, Gaudet et al. [36] comes with an article which discusses the correlation between the plasma concentration of the marker MMP 9 (matrix metalloproteinase) and POCD in patients that undergo endarterectomy. MMP 9 being a proteolytic enzyme that acts on the progression and destabilization of atheromatous plaques contributes to damage to the blood-brain barrier and contributes to the formation of cerebral edema, resulting in cerebral ischemia. Increased MMP 9 preoperatively correlated with patients who developed POCD. There were no increases in postoperative MMP 9 values. Thus, the authors recommend the use of MMP 9 as a predictor of POCD.

Other evaluation methods

Cerebral oximetry is based on Beer-Lambert's principle, where the concentration of a substance can be measured according to the degree of light absorption. Regardless of the factors that act on the human body in causing cognitive dysfunction, ultimately the brain suffers through hypoxigenation, ischemia, and as a consequence the onset of POCD. The variety of studies, were performed in both cardiac and non-cardiac surgery. Thus, Murkin J. et al. [52] makes a hypothesis that controlling oxygen concentration in the brain during heart surgery by the method of brain oximetry monitoring would have beneficial effects on systemic organs. As a result, Murkin J. asserts that monitoring and modulating intraoperative conduction based on cerebral oximetry values in coronary bypass patients avoids profound brain desaturation and is associated with fewer major organ dysfunction. However, the given method suffers from some limitations, the monitoring of cerebral oximetry does not continue in the ICU (intensive care unit), brain oxyge-nation is performed on a small part of the brain and may be influenced by anatomic particularity or cerebral edema.

Another study by Slater J. et al. [53], in patients to be operated in cardiac surgery, prolonged intra-operative cerebral desaturation has an increased risk of developing POCD and prolongs in-hospital stay.

Casati A. et al. [54] in his study uses brain oximetry monitoring in major abdominal surgery in elderly patients. The results are to show that intraoperative adjustment of cerebral oximetry and avoidance of cerebral desaturation prevents cerebral ischemia in elderly patients, thus preventing the onset of POCD and shortens the patient hospital stay, approaching the discharge period.

Critical analysis of POCD study methodologies in publications

In spite of the fact of the years of study in the unraveling of POCD, many questions remain unclear. In 2013, Uysal S. and Reuch D. [55] confirmed that the difficulty relates to a number of factors, including very different methods of POCD assessment, and variations in surgical management and surgical techniques over time. The sensitivity, specificity, and overall usefulness of neurocognitive research methods are well established, but the application of these methods to cardiac surgery over the past 30 years has often been mistaken.

In 2007, Newman S. et al. [27] comes with a study based on investigations of POCD-related publications in non-cardiac surgery. The authors assert that no study was able to elucidate the possible mechanisms in the occurrence of POCD. Research suffers from major shortcomings in the number of studies in the field and a number of other technological difficulties. This includes the high variability of the type of surgery and anesthesia, the number of patients enrolled in the study, the diversity of recruitment, the variability of neuropsychological tests with different sensitivity, the diversity of statistical analysis, and even the variety of application of the definition used in the classification of study participants as POCD. These differences make it difficult to compare studies with each other.

Rasmussen L. et al. [17] asserts that the low frequency of POCD in some studies is caused by the incorrect methodology chosen to detect cognitive deviations. Using lower threshold tests will not show the presence of POCD correctly. Using easy memorable tests will result in underestimations, and obtaining the same postoperative outcome in comparison with the pre-operative shows certainly that POCD has taken place, which many authors do not take into account.

Conclusions

Postoperative cognitive dysfunction is a common complication after the surgery. It occurs in frail patients or in individuals presenting general risk factors. It looks like there is a genetic predisposition for the development of postoperative cognitive dysfunction. Patients at risk of postoperative cognitive dysfunction can be identified by neurocognitive testing tools.

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Declaration of conflicting interests
Nothing to declare.