

Original article

Impact of Anesthesia on the Development of Postoperative Delirium

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SUMMARY

Introduction/Aim. Postoperative delirium is defined as an acute state of confusion that develops within hours or days after surgical intervention. With the global aging of the world population, the number of geriatric patients who will undergo surgery is on a steady rise, increasing therefore the possibility of postoperative delirium. The primary aim of this study was to determine the effect of age, type of surgical procedure, as well as the type of anesthesia on postoperative delirium.

Methods. The investigation was performed in the form of a prospective study. Patients who underwent general and regional anesthesia were included. Benzodiazepines and atropine were used for premedication; from among intravenous anesthetics, propofol was used for hypnosis and from inhalation anesthetics sevoflurane; for analgesia, opioids were used. Bupivacaine was used to administer regional anesthesia. The level of cognitive functioning was tested using two tests: the Mini Mental Examination in the preoperative period and the CAM-ICU in the postoperative period.

Results. Using the t-test for independent samples, it was found that there was a statistically significant difference between the two age groups of patients. It was found that there was no statistically significant difference in terms of cognitive functioning between patients who received general anesthesia and those who received regional anesthesia. The results of the analysis showed that there was no statistically significant difference between groups who received different types of surgery.

Conclusion. The practical value of this study is that the preparation of patients for these types of abdominal interventions can follow the general guidelines.

Keywords: anesthesia, delirium, elderly patients

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INTRODUCTION

Postoperative delirium is defined as an acute state of confusion that develops within hours or days after surgical intervention, and is not an uncommon complication in geriatric patients undergoing extensive surgery (1). As early as 1955, Bedford was the first to observe that cognitive impairments could be associated with the use of anesthetics in elderly patients. This finding highlighted the importance of these disorders because they could complicate and slow down the process of recovery after surgery (2). The entire process of therapeutic and surgical treatment of a geriatric patient can be compromised and endangered if cognitive dysfunction remains a persistent problem after the patient is discharged from the hospital.

With the global aging of the world population, the number of geriatric patients who will undergo surgery is on a steady rise, increasing therefore the possibility of postoperative cognitive complications as well (3). Half of all surgical procedures are performed on patients over the age of 65, which further increases the risk of cognitive complications. In the population over 65 years of age, cognitive problems are rather common; 10% of people over the age of 65 have some cognitive impairment, while 40% to 50% of those over the age of 85 meet the criteria for dementia (4).

The pre-existing comorbid conditions increase the risk of postoperative complications. Therefore, elderly patients may benefit significantly from preoperative assessment of cardiac, respiratory, hematological, and renal function. It has been documented that the preoperative presence of cognitive impairment increases the risk of postoperative complications, including confusion and memory deficits (5). However, there is still no routine preoperative cognitive assessment available. Risk factors for the development of postoperative delirium are numerous and depend on the characteristics of individual patients, surgery-related factors and anesthesiological factors (6).

The detection of patients who are at increased risk and proper recognition of the clinical picture of delirium is becoming an important component in the care of geriatric surgical patients (7). If delirium is allowed to go on unrecognized and is not adequately treated, it may increase postoperative complications, prolong the duration and cost of hospitalization, and can have long-term consequences on patients' cog-

nitive status and aspects of quality of life (8). The rate of cognitive complications among geriatric surgical patients is significant, making it a problem that attracts the attention of the health system in the preoperative, perioperative, and postoperative periods. Between 20% and 46% of patients over 65 years of age undergoing non-cardiac surgery experience postoperative delirium.

Postoperative delirium is manifested by the classic clinical signs of delirium – acute confusion during the first hours and days after surgery, attention deficits, and disorganized thinking that fluctuates over a number of hours or changes throughout the day (9). Patients often have a disturbance in the circadian rhythm and the rhythm of wakefulness and sleep. Postoperative delirium takes place in the following three forms:

- Hyperactive: the patients are agitated and often require sedation and measures of physical restraint.
- Hypoactive: the patients are lethargic and drowsy, and are at risk of being overlooked by medical staff.
- Subsyndromal: the patients are unrecognized during the postoperative period and should be considered, since a large proportion of patients with postoperative delirium later tend to develop dementia.

The American Geriatrics Society recently published an easy-to-implement practical guide that should standardize surgical procedures for geriatric patients undergoing surgery, which could help reduce the rate of postoperative delirium.

Delirium should be considered as a result of the interaction between predisposing patient-related risk factors and physiological stress (10). Risk factors for the development of postoperative delirium are well defined and include: age of the patient over 65 years, presence of cognitive impairments or dementia, visual and hearing impairments, significant comorbidities, and coexisting infections.

For patients undergoing non-cardiac surgery, additional risk factors for developing postoperative delirium include functional dependence, excessive alcohol use, and laboratory abnormalities, especially electrolyte imbalances (11). Patients who have two or more risk factors are considered to be more likely to develop postoperative delirium. The risk is higher with emergency surgical interventions than with elective procedures (12).

AIM

The primary aim of this study was to determine the effect of age, type of surgical procedure (with a focus on abdominal procedures), as well as the type of anesthesia (regional and general anesthesia) on postoperative delirium.

METHODS

Draft of the study

The investigation was performed in the form of a prospective study, where the eligible patients from the Clinic for General Surgery and the Clinic for Anesthesia and Intensive Care, University Clinical Center Niš were enrolled. The studied population involved patients admitted to hospital between January 1, 2023 and January 1, 2024. For the effect of age to be tested, patients were divided into two age cohorts, with the first group made up of patients aged 40 to 65 years and the second of those over 65 years of age (the studied types of surgical procedures are performed in significantly fewer cases on patients under 40 years of age, and they are not considered here). Analysis and statistical processing of data from anesthesia charts and medical histories of surgically treated patients were performed.

Exclusion and inclusion criteria

The total number of patients who received anesthesia during this period was 1,855, with this number further narrowed down based on the following criteria:

- Only patients who had undergone surgery for inguinal hernia, gallbladder and perianal abscess were included.

- Patients who had underwent general and regional anesthesia were included. Benzodiazepines and atropine were used for premedication; from among intravenous anesthetics, propofol was used and from among inhalation anesthetics sevoflurane was used for hypnosis; and for analgesia, opioids (fentanyl) were used. Bupivacaine was used to administer regional anesthesia.

- Patients with a previous history of cognitive dysfunction (e.g., preoperative dementia, Korsakoff syndrome, Alzheimer's disease, etc.) were excluded

as this constituted a significant risk for the development of delirium.

Type of anesthesia

When determining the type of anesthesia for each individual patient, a consultation process involving surgeons, anesthesiologists, and the patient was applied. This is a standard procedure in a given clinical setting.

Assessment of cognitive functioning

The level of cognitive functioning was tested in the preoperative and immediate postoperative periods using two different neuropsychological tests: the Mini Mental Examination in the preoperative period and the CAM-ICU in the postoperative period. The selection of tests was not under the control of the researchers, since it was a standard testing procedure in a given clinical setting, whereby verification of the validity of the approach was performed on the basis of the available literature. The given combination of tests enabled the assessment of different domains of cognitive functioning – executive functions, memory, attention, and cognitive flexibility.

It should be further noted that the study was limited to the assessment of short-term postoperative delirium (three days after surgery) for practical reasons. A control group of 120 subjects was tested after the control sample was collected. The control group included individuals who shared significant demographic characteristics, which was why the age-based matching method was used and the absence of a prior history of cognitive dysfunction was chosen as a relevant factor.

Statistical analysis

Statistical methods from the domain of descriptive and inferential statistics were selected in accordance with the aim of the study. When presenting the results of descriptive statistics, both percentages and frequencies would be used, depending on the nature of the data. Simplicity and comprehensibility of the statistical display were used as the main criteria for selecting the display method. ANOVA and t-test were the predominant choices among inferential methods.

RESULTS

Demographic and general characteristics of the studied patient sample

Our initial data analysis included a descriptive analysis of the demographic and relevant clinical characteristics identified in the total sample of 175 subjects and 120 control group subjects. The average age of the studied subjects was 66 years, with the number of subjects up to 65 years of age, and the number of subjects over 65 being relatively uniform

(n1 = 80 and n2 = 95). The average age of the control group subjects was 64.2 years.

The sample was also uniform by the factor of gender, with 89 male and 86 female examinees. Among these patients, 68% were treated under general anesthesia, while 32% were treated under regional anesthesia. The largest number of subjects were subjected to surgical interventions to treat inguinal hernia (42%), gallbladder problems (36%), and perianal abscess (22%).

The patient characteristics in the studied sample can be seen in Table 1.

Table1. Descriptive analysis of sample and control group

Characteristic	Sample group (n = 175)	Control group (n = 120)
Average age	66 years	64.2 years
Age distribution		
- ≤ 65 years	80	62
- > 65 years	95	58
Gender distribution		
- Male	89	63
- Female	86	57
Type of anesthesia		
- General anesthesia	68%	65%
- Regional anesthesia	32%	35%
Type of surgery		
- Inguinal hernia	42%	48%
- Gallbladder	36%	33%
- Perianal abscess	22%	19%

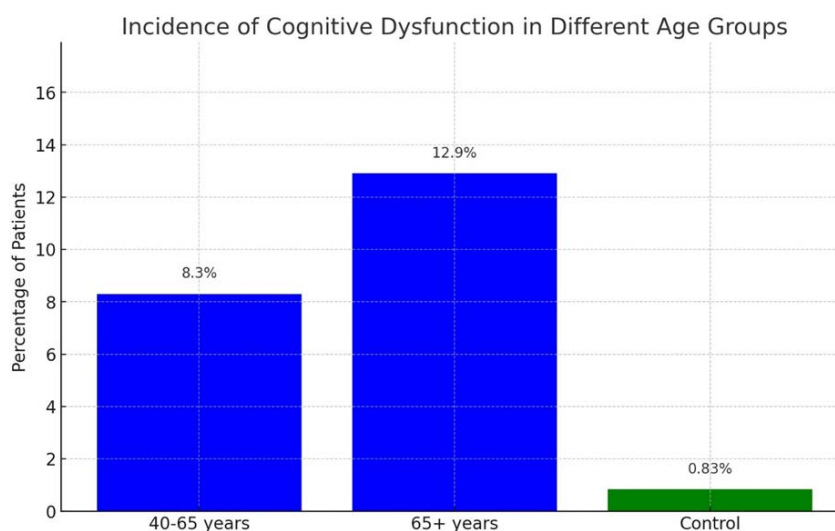


Figure 1. Incidence of postoperative delirium in different age groups

Incidence of postoperative delirium

A simple descriptive analysis found that postoperative delirium occurred in 8.3% of patients aged 40 to 65 years, while in the sample of patients over 65 years of age, delirium was identified in 12.9% of cases. Using the t-test for independent samples, it was found that there was a statistically significant difference between the two groups of patients ($t = 0.57$, $p = 0.006$). Delirium-CAM-ICU testing was also performed in the control group and it was detected to be present in 0.83% (i.e., in one subject), although none of the individuals included in the control group had any of the diagnoses used as the criterion for exclusion from the sample. The T-test for matched samples was applied to the results of the control and study groups and a statistically significant difference was confirmed ($t = 0.89$, $p = 0.001$) (Figure 1.).

Effect of the type of anesthesia

The effect of the type of anesthesia was initially tested using the t-test for independent samples, with the only grouping factor being the anesthesia variable with the categories of general and regional anesthesia, while the age of the patient was not taken into account. Based on the results of the test, it was found that there was no statistically significant difference in terms of cognitive functioning between patients who received general anesthesia and those who received regional anesthesia ($t = 0.678$, $p = 0.552$). In the second step of the analysis, the variables of age (two age cohorts as two separate categories) and the type of anesthesia were crossed. On this data set, the Chi square analysis was applied, and here, too, it was found that the arithmetic means of the scores of cognitive functioning did not differ between the four newly created categories (Chi square = 14.4, $p > 0.05$), (Table 2).

Table 2. *Effect of the type of anesthesia*

Anesthesia type	Total patients	Patients with delirium	Percentage of delirium
General anesthesia	119	14	11.76%
Regional anesthesia	56	5	8.93%

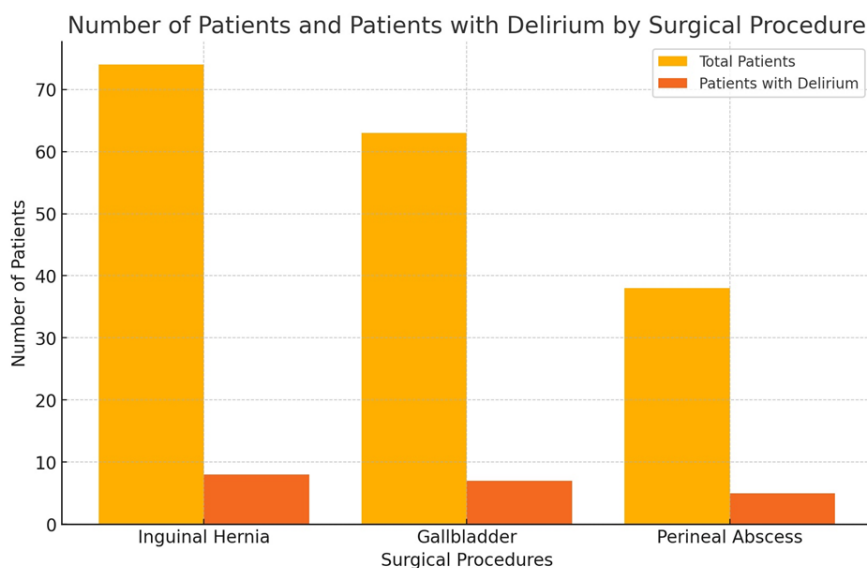


Figure 2. *Effect of surgical procedure*

Effect of the type of procedure

The one-way ANOVA test was used to examine the effect of the type of procedure, where the independent factor was a variable with three categories involving gallbladder, inguinal hernia, and perineal abscess surgery, and the dependent variable was the score on neurological testing. The results of the analysis showed that there was no statistically significant difference between the three categories ($F = 6.67, p > 0.05$). In the second step of the analysis, the variables of the type of surgery and the age of the patient were crossed and it was found that the value of Chi square was not statistically significant (Figure 2).

DISCUSSION

The incidence of delirium depends on the characteristics of the sample and methods used, so it is not surprising that different studies sometimes report rather conflicting results. In some studies, the incidence of delirium varies from 4% to 11%, with subsequent analyses revealing that the differences in percentages can only be descriptively attributed to the type of anesthesia (13). Some studies conducted on large samples have reported a significantly higher incidence among older patients, but a more detailed inspection of the results showed that there were significant variations from hospital to hospital included in the study, which rightly calls into question these figures (14). There are also studies that report findings similar to those obtained in this study. With all this in mind, the results obtained do not deviate from the existing research framework (15).

A significant meta-analysis in this area has shown that there is no statistically significant effect of the type of anesthesia on the development of postoperative delirium in patients after surgery, although some studies show that such an effect in fact exists. However, it should be borne in mind that variability in terms of procedures and types of anaesthesia makes it difficult to reach a conclusion that is applicable in all cases (16, 17). For instance, studies that have studied the effect of epidural and general anesthesia on elderly patients undergoing hip surgery have shown that the claim that epidural anesthesia in these situations is associated with a lower incidence of postoperative delirium is valid on the biological level (18, 19). Such effects of individual procedures may be lost in studies where no dis-

inction is made between surgical procedures, and therefore significantly different results can be obtained. Another study conducted on a large sample of patients who were under general anesthesia showed that in patients over 40 years of age there was not any effect of the type of anesthesia on the occurrence of postoperative delirium (20).

The link between anesthesia and the development of cognitive changes has not been fully elucidated. Most of the available data come from case reports and small prospective studies suggesting that postoperative cognitive deficits occur more frequently after extensive surgical interventions in the OETA, after repeated operations, and when the patient experience perioperative complications (21).

The International Study of Postoperative Cognitive Dysfunction (ISPOCD) found an increased risk with surgical interventions lasting longer than two hours, and recommended that the duration of surgery and anesthesia be limited to one hour whenever possible (22).

The duration of the surgery in our patients ranged from 30 to 120 minutes, which depended on the surgical intervention planned to take place. There was no evidence that anesthesia alone, or any single anesthetic agent, caused postoperative delirium. In general, the shorter the effect of the anesthetic agent, the shorter the duration of cognitive impairment in the postoperative period (23).

One theory is that surgery and anesthesia may affect the neuroinflammatory response, resulting in impaired synaptic transmission in susceptible patients, such as elderly patients or those with previous head injuries. Disruption in central cholinergic neurotransmission during surgical stress and/or direct influence of anesthetics can also occur (24).

Another possibility is that anesthesia is able to alter proteins in the brain, and that this alteration process may contribute to the development of cognitive dysfunction. Exposure to anesthesia was shown to alter the expression of amyloid beta and tau, two proteins associated with Alzheimer's disease and dementia (25).

The results of this study showed that there were no differences in the effects of different types of interventions, which was consistent with the general findings in this area (10, 26). These findings were usually related to non-cardiac surgical interventions.

In patients who have developed symptomatology of postoperative delirium, haloperidol is administered. It is a representative of the first gene-

ration of antipsychotics and a derivative of butyrophenone, an antagonist of dopamine (D2) receptors. In a 2022 clinical practical guide, haloperidol was the first line of choice of antipsychotics recommended for the treatment of delirium, and it still occupies that place today. In patients with the first signs of delirium, haloperidol was administered intramuscularly, fractionally, at a dose of 2.5 mg, up to a maximum daily dose of 10 mg. There were no serious side effects. The symptoms of delirium subsided in an average of 72 hours and the postoperative course and rehabilitation proceeded smoothly.

CONCLUSION

The study of the patients undergoing different types of abdominal interventions demonstrated that the only statistically significant factor influencing the occurrence of postoperative delirium in patients was the age of the patient. Analyses showed that the type of surgery and the type of anesthesia had no effect on the development of delirium. The practical value of this study is reflected in the fact that it has been confirmed by research that the preparation of patients for these types of abdominal interventions can follow the general guidelines regarding the prevention of postoperative delirium and its treatment in cases in which it occurs.

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Article info

Received: June 19, 2024

Accepted: June 25, 2024

Online first: September 26, 2024

Uticaj anestezije na razvoj postoperativnog delirijuma

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SAŽETAK

Uvod/Cilj. Postoperativni delirijum se definiše kao akutno stanje konfuzije koje se razvija u roku od nekoliko sati ili dana nakon hirurške intervencije. Zbog globalnog starenja populacije, broj gerijatrijskih bolesnika koji će biti podvrgnut hirurškim zahvatima u stalnom je porastu, te se povećava mogućnost pojave postoperativnog delirijuma. Primarni cilj ovog istraživanja bio je da se utvrdi uticaj godina, tipa hirurške procedure, kao i tipa anestezije na postoperativni delirijum.

Metode. Istraživanje je sprovedeno u formi prospektivne studije. Uključeni su bolesnici koji su bili podvrgnuti opštoj i regionalnoj anesteziji. Za premedikaciju su korišćeni benzodiazepini i atropin. Od intravenskih anestetika korišćen je propofol za hipnozu, a od inhalacionih sevofluran, dok su za analgeziju korišćeni opiodi. Bupivakain je korišćen za sprovođenje regionalne anestezije. Za ispitivanje nivoa kognitivne funkcionalnosti korišćena su dva testa: test *Mini Mental Examination* u preoperativnom periodu i test *CAM-ICU* u postoperativnom periodu.

Rezultati. Korišćenjem T-testa za nezavisne uzorke utvrđeno je da postoji statistički značajna razlika između dveju starosnih grupa bolesnika. Takođe je utvrđeno da ne postoji statistički značajna razlika u pogledu kognitivnog funkcionisanja između bolesnika kojima je data opšta anestezija i onih kojima je data regionalna anestezija. Rezultati analize pokazali su da ne postoji statistički značajna razlika među grupama koje su bile podvrgnute različitim tipovima hirurških zahvata.

Zaključak. Na osnovu ovog istraživanja može se zaključiti da priprema bolesnika za ove vrste abdominalnih intervencija može pratiti opšta uputstva.

Ključne reči: anestezija, delirijum, stariji bolesnici