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Incidence of postoperative delirium according to cognitive status, improved responsiveness and inflammatory response at elderly patients in urgent abdominal surgery

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Background. Postoperative delirium (POD) is a clinical syndrome that is manifested in impaired consciousness and attention, perception, memory, thinking and psychomotor behavior after surgery.

Methods. After passing the Bioethics Commission at Zaporizhzhya State Medical University and obtaining informed consent from patients, 30 elderly patients who underwent surgical interventions on the abdominal organs under urgent procedure were sequentially included in a single-center prospective study. Patients with a history of traumatic brain injury or stroke with neurological impairments in the form of sensory-motor aphasia and plegia were

excluded from the study.

Results . The study involved 30 patients (16 (53%) women and 14 (47%) men), aged 62 years to 92 years, grade III-IV ASA, who underwent urgent surgery for bowel tumors (n = 8), gallstone disease (n = 7), entrained inguinal and postoperative ventral hernias (n = 10), gastric or intestinal perforation (n = 5). Postoperative delirium occurred in 33% of patients. On the first day after surgery, the cognitive status of patients in the first group decreased by 1 point relative to the primary assessment (p = 0.88), when on the second postoperative day the indicator returned to baseline. Patients in the second group showed a sharp impairment of cognitive abilities in the postoperative period, associated with POD and a significant decrease in cognitive status at day 5 (p <0.05) compared with preoperative assessment. The level of inflammatory response of the body in the preoperative period is 1.5 times higher in patients with POD (p = 0.01). The correlation between leukocytosis level and POD revealed a moderately significant relationship between these indicators (rs = 0.45 at p <0.05).

Conclusions. In 33% of urgent patients, abdominal surgery revealed postoperative delirium, which is reliably dependent on cognitive deficits for surgery and the level of systemic inflammation (p = 0.01). The level of patient wear does not significantly affect the incidence of POD.

Key words: elderly patient; postoperative delirium; cognitive status; urgent abdominal surgery.

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Introduction

Postoperative delirium (POD) is a clinical syndrome that is manifested in impaired consciousness and attention, perception, memory, thinking and psychomotor behavior after surgery [1].

According to a meta-analysis of 11 studies by Scholz and POD co-authors, significantly increases hospital stay and increases hospital mortality [2]. According to Ely E.W. and co-authors, patients who experienced complications in the postoperative period in the form of POD, were in the hospital for 10 days longer than patients whose delirium did not develop [3].

Postoperative delirium has a non-specific etiology. Its development is influenced by a number of factors, which are divided into two groups: favorable and provocative [4]. Favorable factors include old age, male gender, hearing and vision impairment, dementia, reduced cognitive status, functional impairment or deterioration of the body, comorbidity, and alcohol abuse [4,5,6]. Among the provoking factors, the following factors play a significant role: pain, type of surgery, type of anesthetic care, anemia, severity of inflammatory process, metabolic disorders, use of anticholinergic drugs and benzodiazepines [5,4].

According to Marcantonio E. R. POD, it is one of the most common postoperative complications in elderly patients [7]. The more favorable factors the elderly patient has in the preoperative period, the less the number of provoking factors causes the occurrence of POD.

Data on the incidence of POD in elderly patients vary and range from 3-75%. Postoperative delirium complications occur in 3% of patients who underwent routine low-risk surgery [8]. And Milstein and colleagues report that POD develops in 4.4% of elderly patients, even after low-risk cataract surgery [9]

According to Marcantonio E R., delirium frequency from 9% to 25% [7] has been observed in planned elderly patients after low- and moderate-risk surgery [7]. And patients after high-risk surgery had POD in 50% of cases [8, 10]. According to the results of Robinson T.N. and co-authors, POD occurs in 44% of patients over 60 years old after major surgery in abdominal and thoracic surgery, and initial cognitive dysfunction was a major predictor of its development [11]. According to L. Ansaloni and co-authors, postoperative delirium occurs in 13, 2% of planned elderly patients and in 17, 9% of urgent patients [12]. In patients undergoing intensive care, the incidence of POD reaches 75% [13]. According to Freddi Segal-Gidan, the incidence of POD is greater when performing emergency surgery, compared with routine surgery [14].

Considering the heterogeneity of data on the incidence of POD in urgent elderly

patients, the purpose of our study was to evaluate the incidence of POD and to determine its relationship with cognitive status, level of wear and inflammatory response in elderly patients with surgical abdominal surgery.

Materials and methods:

After passing the Bioethics Commission at Zaporizhzhya State Medical University and obtaining informed consent from patients, 30 elderly patients who underwent surgical interventions on the abdominal organs under urgent procedure were sequentially included in a single-center prospective study. Patients with a history of traumatic brain injury or stroke with neurological impairments in the form of sensory-motor aphasia and plegia were excluded from the study. The initial assessment of cognitive status was performed using the Mini-Cog scale [15]. The level of wear was determined on the Frailty scale [16], which took into account the following indicators: number of comorbidities, Mini-Cog score, albumin or total protein level, hematocrit, need for assistance with routine household activities, falls over the last six months. Delphi scale was used to determine the risk of delirium, it includes: age, physical activity, alcohol abuse, history of delirium, hearing impairment, urgency of intervention, open surgery, stay in intensive care [17]. During the first five days after surgery, they performed a daily cognitive status assessment on the Mini-Cog scale at nine o'clock in the morning to create identical assessment conditions and observe daily rhythms. Assessment of sedation and agitation was performed on the Richmond scale [18], which consists of 10 levels (-5 to +4), according to which the level +4 corresponds to the extreme aggressiveness of the patient, level -5 indicates deep sedation. A calm and alert patient responds to level 0. Screening for postoperative delirium was performed using the Confusion Assessment Method (CAM-ICU) [19], which identifies four indicators, such as severity and wavyness of mental status changes, attention deficit, level of consciousness, and assessment of thinking. To determine the level of inflammatory response were guided by the level of leukocytes in the general blood test.

Statistical analysis was performed using Statistica for Windows version 6.0. Quantitative variables are presented as mean \pm standard deviation for normal data distribution, median and quartile for abnormal. To compare them, the Student's t-test and the Mann-Whitney U-test were used. The correlation analysis of non-parametric data was performed through the Spearman correlation.

Results of the study and their discussion

The study involved 30 patients (16 (53%) women and 14 (47%) men), aged 62 years to 92 years, grade III-IV ASA, who underwent urgent surgery for bowel tumors (n = 8), gallstone disease (n = 7), entrained inguinal and postoperative ventral hernias (n = 10), gastric or intestinal perforation (n = 5). General characteristics of patients are presented in Table 1.

Table 1. General characteristics of patients

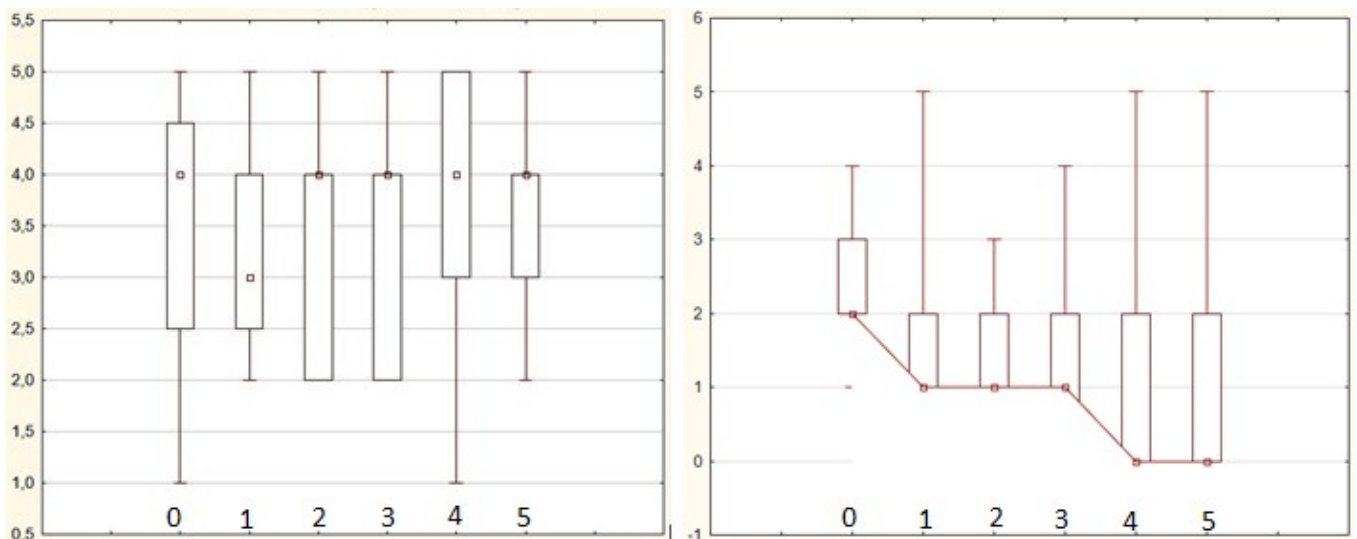
Indicator	Group 1 (n = 20)	Group 2 (n = 10)	p
Age, years	76.5 [68.5; 78.0]	79 [73.0; 87.0]	p = 0,09
Score ASA, class			
II (n)	7	1	
III, n	12	8	
IV, n	1	1	
Fragility, points	3.5 [2.0, 4.0]	4.0 [3.5, 4.0]	p = 0,11
Baseline cognitive impairment scores	4.0 [3.0, 5.0]	2.5 [2.0, 3.5]	p = 0,03
The risk of delirium, points	5,5 ± 2,1	8,1 ± 1,6	p = 0,002
Hb, g / l	119 ± 24	110 ± 29	p = 0,16
The duration of surgery, min	101 ± 56	112 ± 57	p = 0,83
Type of anesthesia			
TBA + ventilator	10	7	
Ca	6	1	
KZEA	4	2	
The duration of mechanical ventilation, min	180 [115.0; 335.0]	437 [160.0, 480.0]	p = 0,06
Length of stay in VAIT, h	24 [24.0; 24.0]	264 [192.0, 288.0]	p = 0,01
Length of hospital stay, days	12.0 [10.0; 15.0]	15.0 [13.0; 21.0]	p = 0,07
Relaparotomii, n	0	4	NS

Note: TBA + IVL - total intravenous anesthesia with artificial ventilation, CA- spinal anesthesia, KSEA - combined general-epidural anesthesia

Postoperative delirium occurred in 33% of patients. No significant age difference was found between the groups. Patients with POD had a greater level of wear and tear than patients without delirium, but no significant difference (p = 0.11) and higher grade than ASA.

Moderate cognitive impairment was detected in patients without delirium in the preoperative period, as opposed to patients with delirium who had severe cognitive impairment ($p = 0.03$). The risk of delirium in patients in the first group was lower by 30% than patients in the second group ($p = 0.002$). The difference in the duration of surgery in patients is not significant. A two-fold increase in the time spent on ventilation was observed in patients with POD ($p = 0.06$). The length of stay of elderly patients with POD in intensive care units exceeds 10 times the length of stay of patients of the first group ($p = 0.01$). Relaparotomy due to surgical complications (bleeding, anastomosis failure) was observed in 4 cases. Hospital mortality of patients with POD was 18%.

The assessment of cognitive status is presented in **Figure 1**.



a) Patients without POD

b) Patients with POD

Figure 1. Cognitive status of patients

Note: along the X-axis, the numerical assessment of cognitive status, along the Y-axis, the day on which the assessment was performed. 0- preoperative assessment of cognitive status, 1- first day after surgery, 2- second day after surgery, 3 - third day after surgery, 4 - fourth day after surgery, 5 - fifth postoperative day. Data are presented as the median and 25-75% of the quartile.

On the first day after surgery, the cognitive status of patients in the first group decreased by 1 point relative to the primary assessment ($p = 0.88$), when on the second

postoperative day the indicator returned to baseline. In patients without POD, the assessment of cognitive ability on day 5 after surgery did not differ from preoperative status ($p = 0.75$). Patients in the second group showed a sharp impairment of cognitive abilities in the postoperative period, associated with POD and a significant decrease in cognitive status at day 5 ($p < 0.05$) compared with preoperative assessment.

The level of leukocytosis is presented in **Table 2**

Table 2. The level of leukocytosis

Indicator	Group 1 (n = 20)	Group 2 (n = 10)	p
'Leykotsyty, × 10 ⁹ / L	8.3 [4.8; 10.0]	14.0 [10.9; 15.6]	p = 0,01
"White blood cells, × 10 ⁹ / L	5.0 [4.5; 8.2]	14.15 [9.0; 16.2]	p = 0,02
'''White blood cells, × 10 ⁹ / L	8.6 [6.4; 11.4]	12.8 [12.2; 14.0]	p = 0,05
''''Whiteblood cells, × 10 ⁹ / L	6.4 [6.3; 8.6]	8.9 [5.0; 10.1]	p = 0,1

Note: '- the level of white blood cells before surgery; ''- level of leukocytes in 1 postoperative day;'''- the level of white blood cells on postoperative day 3;'''' - the level of white blood cells for 5 postoperative days.

The level of inflammatory response of the body in the preoperative period is 1.5 times higher in patients with POD ($p = 0.01$). The correlation between leukocytosis level and POD revealed a moderately significant relationship between these indicators ($r_s = 0.45$ at $p < 0.05$).

POD is a nonspecific polyetiological clinical syndrome, its development depends on a set of provoking and risk factors at all stages of the patient's perioperative management [4]. In the preoperative period, age, multimorbidity, dehydration, hypo or hypernatremia, use of anticholinergic drugs and benzodiazepines are noted. Intraoperative risk of delirium is increased by hypotension, anemia, hypovolemia. After surgery, POD can provoke pain, the use of narcotic analgesics and benzodiazepines, anemia, sepsis [4]. According to Nadelson M R, the urgency of surgery significantly increases the risk of delirium and prolonged cognitive impairment [20].

Multimorbidity, reduced functional status, and patient wear have been recognized as major factors complicating surgery and reducing the ability to deal with stress, making the patient vulnerable to postoperative complications, including POD. [21].

V.V. Likhvantsev and co-authors interpret that it is the previous dementia and reduced cognitive status that are the main factors that lead to POD [22].

At present, there is no single hypothesis for the development of POD which needs further research. A major role in pathogenesis is played by the imbalance of neurotransmitters, including excess catecholamines and phenylalanine, imbalances of serotonin, tryptophan, melatonin, and reduced acetylcholine stores [23].

The clinical picture of POD can change throughout the day and range from hypoactivity (eg., apathy, impaired locomotor activity) to hyperactivity (eg. agitation, increased arousal, and aggression). Mixed delirium subtype is a simultaneous presence of signs of both hyperactivity and hypoactivity. The manifestations of delirium, according to some authors, remain undetermined in more than half of clinical cases due to the fact that the hypoactive form of delirium usually goes unnoticed. Some facts suggest that certain risk factors, such as prior cognitive impairment, older age, wear and tear and severity of physical illness, are more associated with hypoactive delirium [24]. More systematic studies are needed to clarify the relationship between predisposing factors and motor profile.

According to a number of studies, the correction of provocative and risk factors will lead to a reduction in POD by 30% to 40% [25], which leaves open the question of prevention of postoperative delirium, especially in elderly patients.

Conclusions. In 33% of urgent patients, abdominal surgery revealed postoperative delirium, which is reliably dependent on cognitive deficits for surgery and the level of systemic inflammation ($p = 0.01$). The level of patient wear does not significantly affect the incidence of POD.

Research prospects. In the future it is planned to choose the tactics of perioperative management of urgent elderly patients in abdominal surgery depending on the assessment of the risk of postoperative delirium

Conflict of interests. The authors declare no conflict of interest in the preparation of

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