

The risk factors for cognitive dysfunction in elderly patients after laparoscopic surgery

A retrospective analysis

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Abstract

Postoperative cognitive dysfunction (POCD) is very common in clinical settings, it is necessary to analyze the risk factors for POCD in elderly patients after laparoscopic surgery to provide insights into clinical surgery management.

Elderly patients undergone laparoscopy between September 1, 2018 and March 31, 2020 were included. The mini-mental state examination (MMSE) scale was used to evaluate the POCD, and the characteristics and clinical data of patients with and without POCD were collected and compared. Logistic regression was used to analyze the potential influencing factors.

A total of 572 patients with laparoscopic surgery were included. The incidence of POCD was 11.89%. There were significant differences in the history of cerebral infarction, preemptive analgesia, preoperative use of dexmedetomidine, general anesthesia combined with continuous epidural block, duration of surgery, low SpO₂ during anesthesia induction, PaCO₂ after pneumoperitoneum, postoperative PCEA and VAS score at the third day after operation (all $P < .05$). Logistic regression analysis revealed that history of cerebral infarction (OR3.12, 1.02~5.13), low SpO₂ during anesthesia induction (OR2.03, 1.19~4.47), Longer duration of surgery (OR1.82, 1.01~3.16) were risk factors for POCD in elderly patients with laparoscopic surgery, while postoperative PCEA (OR0.43, 0.01~0.91), General anesthesia combined with continuous epidural block (OR0.59, 0.04~0.87), preoperative use of dexmedetomidine (OR0.70, 0.08~0.94) and preemptive analgesia (OR0.75, 0.13~0.90) were the protective factors for POCD in elderly patients with laparoscopic surgery.

For the elderly patients undergoing laparoscopic surgery, the health care providers should be fully alert to the POCD based on those relevant factors.

Abbreviations: BMI = body mass index, MMSE = Mini-mental State Examination, PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, POCD = Postoperative cognitive dysfunction, VAS = visual analogue scale.

Keywords: cognitive dysfunction, elderly, laparoscopic, management, nursing, surgery

1. Introduction

Postoperative cognitive dysfunction (POCD) refers to postoperative mental disorder, anxiety, personality changes, and

memory impairment in patients without mental abnormalities before surgery, which is a central nervous system complication after surgery.^[1] It is been found that patients with cardiovascular surgery had a higher incidence of postoperative cognitive impairment.^[2,3] With the deepening of the research, it has found that POCD also has a certain incidence in patients with non-cardiovascular surgery. Several studies^[4,5] have found that the incidence of POCD in non-cardiac surgery under general anesthesia vary from 3.5% to 25.8%. With the aging of the population becoming more and more serious, the proportion of elderly patients undergoing surgery is gradually increasing, and POCD is also gradually becoming a hot spot in recent years. The current research on POCD mainly involves various fields such as etiology, influencing factors and treatment. However, the pathogenesis of POCD is not yet fully understood.^[6] A series of factors such as perioperative anesthesia medication, anesthesia method selection and management, and postoperative analgesia may affect the occurrence of POCD.^[7,8] Therefore, further investigations on those issues are needed.

Laparoscopic surgery is a newly developed minimally invasive approach for surgery. With regards to its small incision and trauma, less patient's postoperative pain, shortened duration of the hospital stay, and equal therapeutic effect compared to open surgery, laparoscopic surgery is very popular in current clinical settings.^[9,10] With the advancement of laparoscopic technology, in recent years, laparoscopy has been widely carried out in patients of all ages, and its impact on POCD has gradually been paid attention to. Previous studies^[11,12] have raised some

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This study complied with the "Helsinki Declaration" and the relevant regulations of China clinical trial research, and has been approved by the hospital ethics committee (No2018110977-a). All included patients had signed the written informed consent.

The authors declare that they have no competing interests.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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potential factors that have an impact on POCD in the perioperative period. Especially for the elderly patients with surgery, they often have more basic diseases, the organ function gradually declines, the tolerance to surgery and anesthesia decrease accordingly, thus they are more sensitive to the factors that may affect the cognitive function.^[13,14] Based on literature review, we have found that most previous reports^[15,16] were focused on the POCD in patients undergone cardiovascular surgery, but very few on the patients with laparoscopic surgery. Therefore, we aimed to analyze the risk factors for POCD in elderly patients after laparoscopic surgery, to provide evidence for clinical management of laparoscopic surgery.

2. Methods

2.1. Ethical issues

This study complied with the “Helsinki Declaration” and the relevant regulations of China clinical trial research, and has been approved by the hospital ethical committee (No2018110977-a). All included patients had signed the written informed consent.

2.2. Patients

Elderly patients undergone laparoscopy in our hospital between September 1, 2018 and March 31, 2020 were identified as potential participants. The inclusion criteria for included patients were: elderly patients ≥ 60 years old; The patients were evaluated by the Mini-mental State Examination (MMSE) scale^[17] before operation, and it was confirmed that the preoperative cognitive function was normal; well-informed and agreed to participate in this study. Exclusion criteria in this present study were: patients who took long-term medications that may affect mental state; patients with mental disorders; patients with language and visual impairments that cannot communicate normally and cannot cooperate with the examination; Patients who refuse to participate in this study.

2.3. Diagnostic criteria

The diagnosis of POCD complied with the “Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Disorders” developed by the Dementia and Cognitive Impairment Group of the Chinese Academy of Neurology. Clinicians with relevant experience and rigorous training were responsible for the assessment, and the assessment personnel were relatively fixed. The MMSE scale was evaluated once every 2 days before surgery and 3 days after surgery. If the postoperative score decreased by more than 2 points compared with the preoperative score, it was regarded as a decrease in postoperative cognitive function. The MMSE scale included 19 items, which was divided into 5 parts: memory, orientation, attention, calculation, and language ability. If the answer is correct, the score was 1, and if the answer is incorrect or unknown, it was scored as 0. The total score ranged from 0 to 30. The higher the score, the better the patients cognitive ability.

2.4. Data collection

The general information of patients was collected and analyzed, including gender, age, education level, surgery history, body mass index (BMI), diagnosis of diseases. Furthermore, the related perioperative data were collected, including basic diseases such as

hypertension, diabetes, surgical grade, whether they were preemptive analgesia or used dexmedetomidine before surgery, the anesthesia method, duration of surgery, the SpO₂ during anesthesia induction, intraoperative hypotension, estimated blood loss during surgery, the PaCO₂ after pneumoperitoneum, postoperative patient controlled epidural analgesia (PCEA), postoperative patient controlled intravenous analgesia (PCIA), visual analogue scale (VAS) score at the first and third day after operation. Two investigators collected and double-check the collected data, and any disagreement was solved by further discussion.

2.5. Statistical analysis

We use SPSS 23.0 software to analyze the related data. The binary data in this study were expressed as ratio, and the corresponding comparison between 2 groups was tested by Chi-Squared test. The continuous data was expressed as mean \pm standard deviation ($\bar{x} \pm s$), and the corresponding comparison between groups was tested by *t* test. Logistic regression was used to analyze the potential influencing factors. $P < .05$ was considered statistically significant.

3. Results

3.1. The characteristics of included patients

A total of 572 patients with laparoscopic surgery were included. Among them, 68 patients were diagnosed with POCD, the incidence of POCD was 11.89%. As Table 1 presented, there were no significant differences in the gender, age, BMI, operation history, education level and disease diagnosis among patients with and without POCD (all $P > .05$).

3.2. The clinical information of POCD and no- POCD patients

As Table 2 showed, there were significant differences in the history of cerebral infarction, preemptive analgesia, preoperative use of dexmedetomidine, general anesthesia combined with continuous epidural block, duration of surgery, low SpO₂ during anesthesia induction, PaCO₂ after pneumoperitoneum, postoperative PCEA and VAS score at the third day after operation (all $P < .05$), and no statistical differences on the anemia, hypertension, hyperlipidemia, diabetes, surgical grading, intraoperative hypotension, postoperative PCIA and VAS score at the first day after operation were found (all $P > .05$).

3.3. Logistic regression analysis

The statistically different factors among 2 groups in Table 2 were used as independent variables, which were substituted into the multi-factor logistic regression analysis model. The conditional method was used to gradually establish the regression model based on the results of conditional parameter likelihood ratios. Logistic regression analysis revealed that history of cerebral infarction (OR3.12, 1.02~5.13), low SpO₂ during anesthesia induction (OR2.03, 1.19~4.47), Longer duration of surgery (OR1.82, 1.01~3.16) were risk factors for POCD in elderly patients with laparoscopic surgery, while postoperative PCEA (OR0.43, 0.01~0.91), General anesthesia combined with continuous epidural block (OR0.59, 0.04~0.87), preoperative

Table 1**The characteristics of included patients.**

Items	POCD patients (n=68)	No- POCD patients (n=504)	t/ χ^2	P
Male	45 (66.18%)	318 (63.10%)	1.129	.085
Age (y)	67.03±6.22	66.86±7.03	8.170	.102
BMI	26.27±3.01	26.09±2.79	5.114	.137
First operation	59 (86.76%)	452 (89.68%)	1.131	.096
Education level				
Junior school	20 (29.41%)	150 (29.76%)	1.155	.081
Senior school	29 (42.65%)	212 (42.06%)		
Bachelor	11 (16.18%)	85 (16.87%)		
Graduate	8 (11.76%)	57 (11.31%)		
Disease diagnosis				
Gallstone	19 (27.94%)	149 (29.56%)	1.027	.057
Appendicitis	17 (25%)	120 (23.81%)		
bile duct stones	13 (19.12%)	94 (18.65%)		
Digestive tract perforation	9 (13.24%)	62 (12.30%)		
Gastrointestinal cancer	6 (8.82%)	45 (8.93%)		
others	4 (5.88%)	34 (6.75%)		

Table 2**The comparison on the clinical information of POCD and no- POCD patients.**

Variables	POCD patients (n=68)	No-POCD patients (n=504)	χ^2	P
Anemia	15 (22.06%)	96 (19.05%)	1.038	.101
hypertension	12 (17.65%)	90 (17.86%)	2.630	.095
Hyperlipidemia	19 (27.94%)	132 (26.19%)	1.287	.171
Diabetes	8 (11.76%)	61 (12.10%)	1.022	.304
History of cerebral infarction	11 (16.18%)	28 (5.56%)	1.174	.007
Surgical grading				
ASA I-II	62 (91.18%)	465 (92.26%)	1.205	.098
ASA III	6 (8.82%)	39 (7.74%)		
Preemptive analgesia	3 (4.41%)	162 (32.14%)	3.190	.022
Preoperative use of dexmedetomidine	16 (23.53%)	313 (62.10%)	2.773	.009
General anesthesia combined with continuous epidural block	3 (4.41%)	127 (25.20%)	1.135	.047
Duration of surgery				
<2 hours	12 (17.65%)	223 (44.25%)	3.284	.015
2–3 hours	36 (52.94%)	201 (39.88%)		
>3 hours	20 (29.41%)	80 (15.87%)		
Low SpO ₂ during anesthesia induction				
>80%	8 (11.76%)	278 (55.16%)	2.285	.041
60%–80%	52 (76.48%)	192 (38.10%)		
<60%	8 (11.76%)	34 (6.74%)		
Intraoperative hypotension	14 (20.59%)	101 (20.04%)	1.148	.085
Estimated blood loss during surgery (mL)				
<200	35 (51.47%)	260 (51.59%)	3.081	.113
200–500	24 (35.29%)	177 (35.12%)		
>500	9 (13.24%)	67 (13.29%)		
PaCO ₂ (mm Hg) after pneumoperitoneum				
<40	11 (16.18%)	126 (25%)	2.845	.038
40–50	31 (45.59%)	342 (67.86%)		
>50	26 (38.23%)	36 (7.14%)		
Postoperative PCEA	16 (23.53%)	261 (51.79%)	5.169	.025
Postoperative PCIA	25 (36.76%)	187 (37.10%)	1.193	.171
VAS score at the first day after operation				
<3	27 (39.71%)	194 (38.49%)	2.194	.183
3–5	21 (30.88%)	151 (29.96%)		
>5	20 (29.41%)	159 (31.55%)		
VAS score at the third day after operation				
<3	36 (54.94%)	412 (81.75%)	3.166	.017
3–5	17 (25%)	54 (10.71%)		
>5	15 (22.06%)	38 (7.54%)		

Table 3
Logistic regression analysis on the influencing factors for POCD in elderly patients with laparoscopic surgery.

Variables	β	SE	OR	95%CI	P	Rank
History of cerebral infarction	0.85	0.24	3.12	1.02–5.13	.024	1
Low SpO ₂ during anesthesia induction	0.91	0.36	2.03	1.19–4.47	.030	2
Postoperative PCEA	1.12	0.41	0.43	0.01–0.91	.042	3
General anesthesia combined with continuous epidural block	0.93	0.30	0.59	0.04–0.87	.033	4
Preoperative use of dexmedetomidine	1.04	0.24	0.70	0.08–0.94	.044	5
Duration of surgery	0.95	0.15	1.82	1.01–3.16	.037	6
Preemptive analgesia	0.74	0.18	0.75	0.13–0.90	.023	7

use of dexmedetomidine (OR0.70, 0.08~0.94) and preemptive analgesia (OR0.75, 0.13~0.90) were the protective factors for POCD in elderly patients with laparoscopic surgery (Table 3).

4. Discussion

Due to the influence of various factors during the perioperative period, the patients with POCD may show a decline in memory, attention and social adaptability within a few days after surgery.^[18,19] The typical clinical manifestations of POCD are anxiety, personality changes, memory impairment, orientation and perception disorders.^[20] POCD can increase the occurrence of postoperative complications and cost of medical resources, and affect the long-term quality of life of patients.^[21] If the disease does not receive timely and effective interventions, it is easy to progress to Alzheimers disease or vascular dementia.^[22] The results of this present study have found that patients with history of cerebral infarction, low SpO₂ during anesthesia induction, longer duration of surgery have higher risks for POCD after laparoscopic surgery, while patients with postoperative PCEA, general anesthesia combined with continuous epidural block, preoperative use of dexmedetomidine and preemptive analgesia may have lower risks for POCD. It is necessary to take corresponding treatment measures for these influencing factors in clinical settings.

The pathogenesis of cognitive dysfunction involves the central nervous system, endocrine and immune system.^[23] The current research on the pathogenesis of this disease mainly focuses on the functional degradation of the central nervous system.^[24] It has been found that changes in the central cholinergic system, neurotransmitters, stress, inflammatory mediators, genes and other factors can cause central neurotransmitter disorders.^[25] Among them, the combination of surgical stimulation, trauma, and anesthesia induction can lead to neurological dysfunction and can induce POCD.^[26] Especially in elderly patients, the functions of tissues and organs of elderly patients gradually decline, their tolerance to surgery and anesthesia decreases accordingly.^[27] Previous study^[28] has reported that the incidence of POCD in elderly patients after receiving general anesthesia can be as high as 20%. With the improvement of peoples living standards and the advancement of endoscopy technology, the attention to the physical and mental recovery of patients after surgery has gradually increased among the health care providers.^[29] Therefore, early clinical intervention in elderly patients with high risk of POCD has become the most effective and economical treatment strategy to prevent the pathological and physiological development of POCD.

Several protective factors should be considered. Dexmedetomidine can effectively reduce the perioperative stress response,

inflammatory irritation and the dose of analgesic drugs. Besides, it has less interference with the central cholinergic system, which helps the recovery of patients postoperative cognitive function.^[30] Furthermore, it has little effect on circulatory function and no respiratory depression.^[31] Previous study^[32] has showed that sedation with dexmedetomidine can significantly reduce the incidence of delirium after surgery. Postoperative PCEA can effectively slow the conduction of low-level sympathetic nerves, and block the transmission of noxious stimuli to the central nervous system, significantly reduce the release of inflammatory factors, and reduce the damage of inflammatory factors to the central nervous system.^[33] Severe postoperative pain affects the recovery of the patient's physiological function, and effective postoperative analgesia can significantly reduce the occurrence of complications.^[34] Preoperative analgesia before surgery is used to inhibit peripheral nerve and central nerve sensitization and maintain a smooth transition during the recovery period of anesthesia.^[35] The use of general anesthesia combined with epidural block anesthesia, through epidural block of spinal nerve roots, can well control the transmission of stimulation signals to the central nervous system.^[36]

Shortening the operation time as much as possible is important for reducing the incidence of POCD. Shortening the operation time not only reduces the trauma and the release of inflammatory mediators, but also effectively reduces the intake of sedative and analgesic drugs.^[37] Factors such as laparoscopic CO₂ pneumoperitoneum should also be concerned. The acidosis caused by CO₂ pneumoperitoneum can affect synaptic nerve function, relax cerebral blood vessels, increase intracranial pressure, then promote the release of vascular factors and actuate-venous short circuit opening, and eventually cause cognitive dysfunction.^[21,38] For example, through reasonable adjustment of breathing parameters, balancing the proportion of lung shunt and ventilation blood flow, and promoting the emission of CO₂, which may effectively improve POCD.

Several limitations in this study should be considered. Firstly, this is a single institution, retrospective analysis of POCD following laparoscopic surgery in China, there may be some biases since our study is a retrospective analysis. Secondly, the small sample size may be not power enough to detect the differences, future studies with larger sample size are needed. Besides, it is necessary to conduct more studies with longer follow-up period to identify the potentially influencing factors in the future.

5. Conclusions

In conclusions, for patients with the influencing factors analyzed in this study, clinicians should be fully vigilant and carry out relevant screening for POCD in time, therefore finding and

intervening as soon as possible to improve the quality of life of elderly patients after laparoscopic surgery. However, the selection of different diagnostic scales on cognition dysfunction may also bias the results. Additionally, limited to medical insurance policies, current serological indicators related to cognitive dysfunction, such as serum S-100 β , cannot be implemented among the groups in this study. Therefore, this study may lack an objective basis and is bound to have certain limitations, future studies to explore more sensitive indicators on the POCD are warranted.

Author contributions

Y F, Y L designed research; Y F, X L conducted research; Y F, S W analyzed data; Y F, Y L wrote the first draft of manuscript; Y L had primary responsibility for final content. All authors read and approved the final manuscript.

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