pISSN: 2508-5778 • eISSN: 2508-5859
Ann Hepatobiliary Pancreat Surg 2023;27:301-306
https://doi.org/10.14701/ahbps.23-012

AHBPS
Annals of Hepato-Biliary-Pancreatic Surgery

Check for updates

Original Article

Postoperative delirium after cholecystectomy in older patients: A retrospective study

Young Mok Park[1], Hyung Il Seo[1], Byeong Gwan Noh[1], Suk Kim[2], Seung Baek Hong[2], Nam Kyung Lee[2], Dong Uk Kim[3], Sung Yong Han[3]

[1]Department of Surgery, Biomedical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea,
[2]Department of Radiology, Biomedical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea,
[3]Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea

Backgrounds/Aims: Postoperative delirium (POD) is a common complication that increases mortality and morbidity in older patients. This study aimed to evaluate the clinical significance of post-cholecystectomy delirium in older patients.
Methods: This retrospective study included 201 patients aged > 75 years who underwent cholecystectomy for acute or chronic cholecystitis between January 2016 and December 2019. Patients were divided into the POD (n = 21) and non-POD (n = 180) groups, and their demographic features and clinical results were compared.
Results: The mean patient age was 78.88 years; the female/male ratio was 44.8%/55.2%. Laparoscopic surgery was performed in 93.5% of patients. The univariate analysis showed that lower body mass index (BMI), immobilized admission status, neuropsychiatric disease history, preoperative intervention (percutaneous drainage), high C-reactive protein, hypoalbuminemia, neutrophilia, hypo-/hyperkalemia, and longer operative time were more frequently observed in the POD group. The multivariate analysis showed that lower BMI (odds ratio [OR], 2.796; p = 0.024), neuropsychiatric disease history (OR, 3.019; p = 0.049), hyperkalemia (OR, 5.972; p = 0.007), and longer operative time (OR, 1.011; p = 0.013) were significant risk factors for POD.
Conclusions: POD was associated with inflammation degree, general condition, poor nutritional status, electrolyte imbalance, and stressful conditions. Recognizing risk factors requiring multidisciplinary team approaches is important to prevent and treat POD.

Key Words: Delirium; Cholecystectomy; Body mass index; Nutrition; Older patients

INTRODUCTION

Postoperative delirium (POD) is a common postoperative complication that increases mortality and morbidity, especially in older patients [1-3]. Delirium is a cognitive disturbance that is characterized by acute and fluctuating impairment in attention and awareness [1-3]. Delirium shows symptoms similar to dementia, a disease that chronically deteriorates brain function; however, when the causative factors are normalized, it is mostly ameliorated [4]. Although the overall incidence of POD has been reported to be 2.5%–3%, it is higher in older patients [5,6]; approximately 10%–50% of patients with advanced age of > 70 years undergoing surgical treatment may develop delirium postoperatively [7-9]. Furthermore, delirium has been associated with higher in-hospital mortality of 4%–17% and post-discharge mortality (22.7%) [2-4]. POD after gastrointestinal surgery has been associated with a 10%–20% risk; however, despite the widespread use of cholecystectomy, there have been few reports of POD after cholecystectomy [10,11]. Therefore, we aimed to evaluate the clinical impact and risk factors of POD after cholecystectomy in older patients.

Received: January 26, 2023, **Revised:** April 1, 2023,
Accepted: April 5, 2023, **Published online:** June 20, 2023

Corresponding author: Hyung Il Seo, MD, PhD
Department of Surgery, Biomedical Research Institute,
Pusan National University Hospital, 179 Gudeok-ro, Seo-gu, Busan 49241, Korea
Tel: +82-51-240-7238, Fax: +82-51-247-1365, E-mail: seohi71@hanmail.net
ORCID: https://orcid.org/0000-0002-4132-7662

MATERIALS AND METHODS

Patients

A total of 201 older patients (aged > 75 years) who underwent cholecystectomy for acute or chronic cholecystitis at Pusan National University Hospital in the period January 2016 to December 2019 were included in the study. A retrospective analysis was performed based on medical records. We compared demographic features and clinical results between the POD group (n = 21) and the non-POD group (n = 180). We excluded cases where additional surgery other than cholecystectomy was performed.

This retrospective study was conducted in accordance with the relevant guidelines and regulations, and complied with the Declaration of Helsinki. It was approved by the Pusan National University Hospital Institutional Review Board at the Clinical Trial Center (Institutional Review Board No. 2111-013-108).

Diagnosis of POD

We used the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM–V) and Confusion Assessment Method (CAM) to evaluate and identify POD. All patients with POD were diagnosed via psychiatric consultations. Table 1 lists the full diagnostic criteria from the DSM–V, and defines the key feature of delirium as a disturbance in attention and awareness [5]. Many assessment tools have been developed to easily and quickly detect and evaluate delirium. The CAM is a screening tool that consists of four features: (a) an acute onset and fluctuating course of mental state, (b) inattention, (c) disorganized thinking, and (d) an altered level of consciousness. Delirium is diagnosed when features (a) and (b) are satisfied essentially, and (c) or (d) selectively [6].

Reference ranges of laboratory data

We defined a high C-reactive protein (CRP) value of over 0.5 mg/dL as the reference range at our institution. Furthermore, low hemoglobin was defined as values below 12.5 g/dL, and hypoalbuminemia was below 3.3 g/dL. Impaired renal function was defined as a creatinine level of > 1.2 mg/dL. Neutrophilia was defined as a neutrophil rate of > 73%. The reference ranges for sodium and potassium were 138–148 mmol/L and 3.5–5.3 mmol/L, respectively. All of these were preoperative results and serum levels.

Management of POD

Our treatment strategy for POD involved two tracts. First, the non-pharmacologic prevention strategy included adequate oxygen delivery and fluid and electrolyte balance correction. Non-pharmacological prevention requires a multidisciplinary team approach. Hence, we provided adequate nutritional intake, and encouraged early mobility. Second, in pharmacologic treatment, it is necessary to treat the causes of delirium, such as postoperative pain and sleep deprivation. Therefore, we administered painkillers, such as non-steroidal anti-inflammatory drugs, opiates, trazodone, and quetiapine, for proper sleep induction. Haloperidol, risperidone, quetiapine, and lorazepam were also administered, if and when the patient developed agitation and hallucinations.

Statistical analysis

Statistical analyses were performed using the SPSS software version 20.0 (IBM Corp.). Continuous variables are presented as the mean ± standard deviation. Intergroup comparisons were performed using the independent t-test or Wilcoxon rank–sum test. The chi-square or Fisher's exact test was used to analyze categorical variables. We demonstrated independent risk factors for POD using logistic regression analysis. Significance was set at $p < 0.05$.

RESULTS

Demographics and surgical outcomes of patients

Table 2 summarizes the patient demographics. The incidence of POD after cholecystectomy was 10.4%. The mean patient age was 78.88 years, and 44.8% of the patients were female. Laparoscopic and open surgeries were performed in 93.5% and 6.5% of patients, respectively. Preoperative interventions, such as endoscopic retrograde cholangiopancreatography and percutaneous

Table 1. Definition of delirium in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [5]

	Diagnostic criteria
A.	A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
B.	The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
C.	An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).
D.	The disturbances in criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
E.	There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

Table 2. Demographic features of the patients

Variable	Total (n = 201)	Non-POD group (n = 180)	POD group (n = 21)	*p*-value
Sex (female)	90 (44.8)	79 (43.9)	11 (52.4)	0.459
Age (yr)	78.88 ± 3.52	78.76 ± 3.49	79.95 ± 3.63	0.140
BMI (kg/m^2)	23.76 ± 2.91	23.94 ± 24.11	22.18 ± 3.87	0.008
Symptoms	129 (64.2)	116 (64.4)	13 (61.9)	0.818
ASA (III, IV)	64 (31.8)	55 (30.6)	9 (42.9)	0.252
Admission status				
Wheelchair/stretch car	76 (37.8)	63 (35.0)	13 (61.9)	0.016
Underlying disease				
Medical disease	162 (80.6)	144 (80.0)	18 (85.7)	0.531
Neuropsychiatric disease	40 (19.9)	32 (17.8)	8 (38.1)	0.027
Preoperative intervention				
ERCP	49 (24.4)	46 (25.6)	3 (14.3)	0.255
PTGBD	74 (36.8)	61 (33.9)	13 (61.9)	0.012
Extended operation	9 (4.5)	8 (4.4)	1 (4.8)	0.947
Lapa (versus open)	188 (93.5)	169 (93.9)	19 (90.5)	0.547
Previous operation	74 (36.8)	64 (35.6)	10 (47.6)	0.278
Positive culture rate				
Blood culture	18 (9.0)	14 (7.8)	4 (19.0)	0.087
Bile culture	74 (36.8)	64 (35.6)	10 (47.6)	0.278
Urine culture	12 (6.0)	9 (5.0)	3 (14.3)	0.089
High CRP[a)]	113 (56.2)	96 (54.5)	17 (81.0)	0.021
Low hemoglobin[b)]	99 (49.3)	87 (48.9)	12 (57.1)	0.474
Hypoalbuminemia[c)]	37 (18.4)	28 (15.6)	9 (42.9)	0.002
Impaired renal function[d)]	23 (11.4)	19 (10.6)	4 (19.0)	0.256
Neutrophilia[e)]	70 (34.8)	57 (31.7)	13 (61.9)	0.007
Hyper-/hyponatremia[f)]	85 (42.3)	72 (40.0)	13 (61.9)	0.057
Hyper-/hypokalemia[g)]	18 (9.0)	12 (6.7)	6 (28.6)	0.001
Operative time (min)	101.40 ± 48.55	98.67 ± 45.99	124.8 ± 63.25	0.019
Hospital stay (day)	4.99 ± 13.22	4.79 ± 13.88	6.67 ± 4.45	0.541
Postoperative morbidity	10 (5.0)	9 (5.0)	1 (4.8)	0.962
Post-discharge mortality	30 (14.9)	24 (13.4)	6 (28.6)	0.066

Values are presented as number (%) or mean ± standard deviation.
BMI, body mass index; ASA, American Society of Anesthesiologist; ERCP, endoscopic retrograde cholangiopancreatography; PTGBD, percutaneous transhepatic gallbladder drainage; Lapa, laparoscopic; CRP, C-reactive protein.
Reference range (serum): [a)]CRP (0–0.5 mg/dL); [b)]hemoglobin (12.5–15.0 g/dL); [c)]albumin (3.3–5.2 g/dL); [d)]creatinine (0.4–1.2 mg/dL); [e)]neutrophil (40%–73%); [f)]Na (138–148 mmol/L); [g)]K (3.5–5.3 mmol/L).

transhepatic gallbladder drainage (PTGBD), were performed in 24.4% and 36.8% of patients, respectively. At admission, 37.8% of patients were immobilized using a wheelchair or stretch car. The American Society of Anesthesiologists status > III was seen in 31.8%. Regarding the history, 80.6% of patients were reported to have any medical disease, while 19.9% had neuropsychiatric diseases. A total of 36.8% of patients had other operative histories.

Table 2 describes the surgical outcomes. The extension rate of surgery due to adjacent organ injury or bleeding was 4.5%. The mean operative time was 101.4 min, and the mean length of hospital stay was 4.99 days. The overall postoperative morbidity (Clavien-Dindo grade III or IV) was 5.0%. The post-discharge mortality rate, not related to surgery, was 14.9%.

Univariate analysis for risk factors of POD

In the univariate analysis, the body mass index (BMI) was significantly lower in the POD group than in the non-POD group (22.18 ± 3.87 vs. 23.94 ± 24.11 kg/m^2, p = 0.008). POD was more frequent in patients using a wheelchair or stretch car than in the mobile ones (61.9% vs. 35.0%, p = 0.016). The rate of neuropsychiatric disease was 38.1% in the POD group, which was significantly higher than that in the non-POD group (17.8%, p = 0.027). Preoperative intervention (PTGBD) was performed more frequently in the POD group than in the non-POD group (61.9% vs. 33.9%, p = 0.012). In addition, preoperative blood tests were different in both groups. High CRP level (> 0.5 mg/dL), hypoalbuminemia, and neutrophila were higher in the POD group (81.0% vs. 54.5%, p = 0.021; 42.9% vs. 15.6%, p = 0.002; and 61.9% vs. 31.7%, p = 0.007, respectively). Electrolyte imbalance, especially serum potassium imbalance, was more frequently observed in the POD group (28.6% vs. 6.7%, p = 0.001). Among the surgery-related factors, the mean operative time was significantly different between the groups (124.80 ± 63.25 vs. 98.67 ± 45.99 min, p = 0.019) (Table 2, 3).

Multivariate analysis for risk factors of POD

In the multivariate analysis, lower BMI (odds ratio [OR], 2.796; p = 0.024), neuropsychiatric disease history (OR, 3.019; p = 0.049), hypo-/hyperkalemia (OR, 5.972; p = 0.007), and longer operative time (OR, 1.011; p = 0.013) were independent significant risk factors for POD after cholecystectomy in older patients (Table 3).

DISCUSSION

Delirium is a cognitive disturbance that is characterized by acute and fluctuating impairments in attention and awareness [1-3]. Compared with dementia, a disease that deteriorates brain function chronically, delirium shows very similar symptoms, but when the causative factors are normalized, is mostly ameliorated [4].

Multiple risk factors for POD have been identified. Pisani et al. [7] presented evidence-based and consensus statements for preoperative, intraoperative, and postoperative risk factors for POD. The preoperative factors were advanced age, comorbidities, preoperative fluid fasting and dehydration, hyponatremia or hypernatremia, and anticholinergic drugs. During surgery,

Table 3. Risk factors for postoperative delirium after cholecystectomy

Variable	Univariate analysis	Multivariate analysis	
	p-value	Odds ratio (95% CI)	*p*-value
Sex (female)	0.46	-	-
Age (yr)	0.14	-	-
BMI (kg/m^2)	0.008	2.796 (1.474–16.49)	0.024
Symptoms	0.82	-	-
ASA (III, IV)	0.25	-	-
Admission status (wheel chair/stretch car)	0.02	0.948 (0.307–2.930)	0.919
Underlying disease			
Medical disease	0.53	-	-
Neuropsychiatric disease	0.03	3.019 (1.003–9.081)	0.049
Preoperative ERCP	0.26	-	-
PTGBD	0.01	0.687 (0.230–2.051)	0.501
Extended operation	0.95	-	-
Lapa (versus open)	0.55	-	-
Previous operation	0.28	-	-
Positive culture rate			
Blood culture	0.09	-	-
Bile culture	0.28	-	-
Urine culture	0.09	-	-
High CRP[a]	0.02	0.618 (0.156–2.449)	0.494
Low hemoglobin[b]	0.47	-	-
Hypoalbuminemia[c]	0.002	0.954 (0.260–3.495)	0.943
Impaired renal function[d]	0.26	-	-
Neutrophilia[e]	0.007	2.701 (0.972–7.506)	0.057
Hyper/hyponatremia[f]	0.06	-	-
Hyper/hypokalemia[g]	0.001	5.972 (1.638–21.760)	0.007
Operative time (min)	0.02	1.011 (1.002–1.020)	0.013
Hospital stay (day)	0.96	-	-

BMI, body mass index; ASA, American Society of Anesthesiologist; ERCP, endoscopic retrograde cholangiopancreatography; PTGBD, percutaneous transhepatic gallbladder drainage; Lapa, laparoscopic; CRP, C-reactive protein; CI, confidence interval.
Reference range (serum): [a]CRP (0–0.5 mg/dL); [b]hemoglobin (12.5–15.0 g/dL); [c]albumin (3.3–5.2 g/dL); [d]creatinine (0.4–1.2 mg/dL); [e]neutrophil (40%–73%); [f]Na (138–148 mmol/L); [g]K (3.5–5.3 mmol/L).

the site of surgery (abdominal and cardiothoracic) and intraoperative bleeding were significant factors for POD. In addition, pain was identified as a postoperative risk factor. Recent studies identified systemic stress and inflammatory response as playing important roles in the development of this condition [10,11].

Based on our study results, we classified the risk factors for POD into several categories. First, the patient's general status at admission was a significant factor. POD was more frequent in admitted patients using a wheelchair or stretch car, than in those who were mobile. In addition, 38.1% of patients with POD had neuropsychiatric diseases; this rate was significantly higher than that in the non-POD group. Second, the severity of inflammation affected the occurrence of POD. Patients with neutrophilia and high CRP levels showed a significantly higher incidence of POD. In addition, poor nutritional status, represented by lower BMI and hypoalbuminemia, increased the occurrence of POD. Electrolyte imbalance, such as hypo-/hyperkalemia, was also a significant risk factor for POD. Finally, perioperative stressful conditions can be induced by preoperative PTGBD insertion or longer operative time, and these factors were also significant contributors to POD. Among these factors, we demonstrated that lower BMI, neuropsychiatric disease history, hyper-/hypokalemia, and longer operative time were independent significant risk factors for POD after cholecystectomy in older patients.

POD commonly occurs between postoperative days (2 and 5) [1-3]. The occurrence of POD prolongs hospital stay by 2–3 days, and intensive care unit stay for 2 days [12-14]. In our study, most patients experienced POD over 2–3 days. We reported POD occurrence based on medical records and medication board. POD is also associated with surgery-related mortality of 7%–10%, compared to 1% recorded in patients without delirium [15]. Several studies have shown that POD is associated with both short- and long-term cognitive impairments [16-18]. The clinical course of cognitive impairment following POD is characterized by an initial decline and prolonged deterioration [16]. One study suggested an association between POD and dementia up to 5 years after delirium [19]. POD is associated with significant functional decline, and a two-to-three times higher risk of requiring care facilities on discharge [20,21].

In our study, patients with POD had longer hospital stays than those without POD, although the difference was insignificant (4.8 vs. 6.7 days, $p = 0.541$). The reason for the long hospital stay for some patients was mostly due to the exacerbation of the underlying disease. In addition, there was some major complication, such as bile leak, pneumonia, and cardiovascular complication. However, there was no significant difference between the two groups at 5.0% vs. 4.8%. However, postoperative mortality was higher in the POD group (13.4% vs. 28.6%, $p = 0.066$), although no significant difference was noted between the two groups. This may be a bias for patients aged > 75 years.

This study has some limitations. Most of the patients were elderly, and had a medical or psychiatric underlying disorder. So, after surgery, when it was thought that the patient was surgically recovered, the patient was transferred to another medical department, or to professional nursing facilities. Almost all patients transferred without full recovery of POD. Therefore, the detailed course of deterioration or improvement of POD could not be precisely confirmed. Most patients were discharged or transferred without resolution of POD during a short hospitalization period.

The management of POD is the same as that of general delirium. The treatment of the precipitating factor is important for POD prevention [22,23]; hence, current management approaches of delirium mainly focus on precipitants. However, if the precipitating factor is surgery, which is inevitable, other approaches should also be considered. Regarding POD prevention, managing the predisposing factors of delirium is essential, and would decrease delirium-associated morbidity and mortality.

In conclusion, cholecystectomy is a relatively safe operation in the surgical field, but the incidence of POD is high in older patients. In addition, POD is associated with the degree of inflammation, general condition, poor nutritional status, electrolyte imbalance, and stressful conditions. Hence, it is important to recognize the risk factors that require multidisciplinary team approaches to prevent and treat POD, especially in high-risk patients.

FUNDING

This work was supported by clinical research grant from Pusan National University Hospital in 2022.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Young Mok Park, https://orcid.org/0000-0002-4165-3054
Hyung Il Seo, https://orcid.org/0000-0002-4132-7662
Byeong Gwan Noh, https://orcid.org/0000-0002-7764-9516
Suk Kim, https://orcid.org/0000-0003-3268-1763
Seung Baek Hong, https://orcid.org/0000-0002-1731-0430
Nam Kyung Lee, https://orcid.org/0000-0003-1972-2719
Dong Uk Kim, https://orcid.org/0000-0002-7208-7753
Sung Yong Han, https://orcid.org/0000-0002-0256-9781

AUTHOR CONTRIBUTIONS

Conceptualization: YMP, BGN, HIS, SK, DUK. Data curation: YMP, BGN, HIS, NKL, SYH. Methodology: YMP, BGN, HIS, SK, DUK. Visualization: YMP, HIS, BGN, SBH, NKL, SYH. Writing - original draft: YMP, HIS, SK, DUK, BGN. Writing - review & editing: YMP, HIS, SBH, NKL, SYH, BGN.

REFERENCES

1. Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA 1994;271:134-139.
2. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. JAMA 2010;304:443-451.
3. Rudolph JL, Jones RN, Rasmussen LS, Silverstein JH, Inouye SK, Marcantonio ER. Independent vascular and cognitive risk factors for postoperative delirium. Am J Med 2007;120:807-813.
4. Norkiene I, Ringaitiene D, Misiuriene I, Samalavicius R, Bubulis R, Baublys A, et al. Incidence and precipitating factors of delirium after coronary artery bypass grafting. Scand Cardiovasc J 2007;41:180-185.
5. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders (DSM-5-TR). 5th ed. APA, 2013.
6. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med 1990;113:941-948.
7. Pisani MA, Murphy TE, Araujo KL, Van Ness PH. Factors associated with persistent delirium after intensive care unit admission in an older medical patient population. J Crit Care 2010;25:540.e1-e7.
8. Tei M, Ikeda M, Haraguchi N, Takemasa I, Mizushima T, Ishii H, et al. Risk factors for postoperative deliriumin elderly patients with colorectal cancer. Surg Endosc 2010;24:2135-2139.
9. Koebrugge B, Koek HL, van Wensen RJ, Dautzenberg PL, Bosscha K. Delirium after abdominal surgery at a surgical ward with a high standard of delirium care: incidence, risk factors and outcomes. Dig Surg 2009;26:63-68.
10. Lee SH, Lim SW. Risk factors for postoperative delirium after colorectal surgery: a systematic review and meta-analysis. Int J Colorectal Dis 2020;35:433-444.
11. Tai S, Xu L, Zhang L, Fan S, Liang C. Preoperative risk factors of postoperative delirium after transurethral prostatectomy for benign prostatic hyperplasia. Int J Clin Exp Med 2015;8:4569-4574.
12. Brown CH 4th, Laflam A, Max L, Lymar D, Neufeld KJ, Tian J, et al. The impact of delirium after cardiac surgical procedures on postoperative resource use. Ann Thorac Surg 2016;101:1663-1669.
13. Scholz AF, Oldroyd C, McCarthy K, Quinn TJ, Hewitt J. Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. Br J Surg 2016;103:e21-e28.
14. Maniar HS, Lindman BR, Escallier K, Avidan M, Novak E, Melby SJ, et al. Delirium after surgical and transcatheter aortic valve replacement is associated with increased mortality. J Thorac Cardiovasc Surg 2016;151:815-823.e2.
15. Raats JW, van Eijsden WA, Crolla RM, Steyerberg EW, van der Laan L. Risk factors and outcomes for postoperative delirium after major surgery in elderly patients. PLOS ONE 2015;10:e0136071.
16. Saczynski JS, Marcantonio ER, Quach L, Fong TG, Gross A, Inouye SK, et al. Cognitive trajectories after postoperative delirium. N Engl J Med 2012;367:30-39.
17. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, et al.; BRAIN-ICU Study Investigators. Long-term cognitive impairment after critical illness. N Engl J Med 2013;369:1306-1316.
18. Monk TG, Weldon BC, Garvan CW, Dede DE, van der Aa MT, Heilman KM, et al. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology 2008;108:18-30.
19. Lundström M, Edlund A, Bucht G, Karlsson S, Gustafson Y. Dementia after delirium in patients with femoral neck fractures. J Am Geriatr Soc 2003;51:1002-1006.
20. Huded CP, Huded JM, Sweis RN, Ricciardi MJ, Malaisrie SC, Davidson CJ, et al. The impact of delirium on healthcare utilization and survival after transcatheter aortic valve replacement. Catheter Cardiovasc Interv 2017;89:1286-1291.
21. Gleason LJ, Schmitt EM, Kosar CM, Tabloski P, Saczynski JS, Robinson T, et al. Effect of delirium and other major complications on outcomes after elective surgery in older adults. JAMA Surg 2015;150:1134-1140.
22. Bellelli G, Mazzola P, Morandi A, Bruni A, Carnevali L, Corsi M, et al. Duration of postoperative delirium is an independent predictor of 6-month mortality in older adults after hip fracture. J Am Geriatr Soc 2014;62:1335-1340.
23. Heymann A, Radtke F, Schiemann A, Lütz A, MacGuill M, Wernecke KD, et al. Delayed treatment of delirium increases mortality rate in intensive care unit patients. J Int Med Res 2010;38:1584-1595.