



Lower risk of postoperative delirium using laparoscopic approach for major abdominal surgery

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Abstract

Background A laparoscopic approach is increasingly being used for major abdominal surgeries and is reportedly associated with a lower incidence of postoperative complications. However, the association of laparoscopic approach and postoperative delirium remains unclear. We aimed to retrospectively investigate risk factors for postoperative delirium after abdominal surgery particularly assessing the association between a laparoscopic approach and postoperative delirium.

Methods We retrospectively studied 801 patients who underwent major abdominal surgery between April 2012 and December 2013. Among these, 181 (22.6%) patients underwent a laparoscopic and 620 (77.4%) patients underwent an open procedure. A Cox proportional hazard model analysis was used to identify risk factors for the development of postoperative delirium or overall survival within 180 days after surgery. Cumulative incidence of postoperative delirium was assessed using a propensity score-matching analysis.

Results Postoperative delirium occurred in 56 patients (7.0%). A Multivariate Cox proportional hazard model analysis revealed that a laparoscopic approach reduced the risk of postoperative delirium [hazard ratio (HR) 0.30, 95% confidence interval (CI) 0.07–0.84, $p = 0.019$]. Postoperative delirium was associated with worse overall survival within 180 days (HR 4.91, 95% CI 1.96–12.22, $p = 0.001$) after adjusting for other confounders using the Cox proportional hazard model analysis. Patients who developed postoperative delirium showed worse outcomes including higher rate of morbidity except delirium ($p < 0.001$), longer hospitalization ($p < 0.001$), and post-discharge institutionalization ($p < 0.001$). After propensity score-matching, cumulative incidence rates of postoperative delirium were significantly lower in the laparoscopic group compared to the open group (30-day cumulative incidence rate, 1.7% vs. 7.8%, $p = 0.006$).

Conclusions The risk of postoperative delirium after major abdominal surgery is reduced using laparoscopic approach. Postoperative delirium should be prevented as it precipitates adverse postoperative events.

Keywords Postoperative delirium · Major abdominal surgery · Laparoscopic approach · Open approach

Abbreviations

ASA	American Society of Anesthesiologists
CI	Confidence interval
HR	Hazard ratio
ICU	Intensive care unit
SD	Standard deviation

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Postoperative delirium is a frequently encountered complication in clinical practice, ranging between 5% and 15% of all operative procedures [1]. Reportedly, it increases the incidence of postoperative morbidity and mortality and causes functional and cognitive decline [1–4]. The length of hospitalization and hospital costs are found to be higher in patients who develop postoperative delirium compared

to those who do not [2, 5, 6]. Previous studies reported that the incidence of postoperative delirium was influenced by predisposing factors including age [4, 5, 7, 8], history of delirium development [4], cognitive decline [5, 6], pre-existing medical comorbidities [5, 6], psychiatric disease [5], and precipitating factors including surgical procedures such as gastrointestinal surgery [9], hepato-biliary-pancreatic surgery [9], and intensive care unit (ICU) admission [7].

A laparoscopic approach is being increasingly used for major abdominal surgeries including upper gastrointestinal, colonic, and hepato-biliary-pancreatic surgeries and is known to reduce the postoperative complications including cardiopulmonary events, sepsis, and wound infection [10–13]. We hypothesized that the use of a laparoscopic approach also reduces the incidence of postoperative delirium. However, the association between a laparoscopic approach and postoperative delirium remains unclear.

The aim of this study was to evaluate the risk of postoperative delirium after major abdominal surgery focusing on the differences between a laparoscopic and open approach.

Methods

Patients

Between April 2012 and December 2013, 1666 consecutive patients underwent elective or emergency abdominal surgery under general anesthesia at the Asahi General Hospital. Among these, 801 patients underwent major abdominal surgery via an open or laparoscopic approach for esophageal, stomach, colon/rectum, liver, and/or pancreas resection for benign/malignant disease. Patients who underwent less invasive abdominal surgery including cholecystectomy ($n=351$), appendectomy ($n=204$), stoma construction or closure ($n=91$), vascular surgery ($n=74$), ileus surgery ($n=72$), gastrojejunostomy ($n=48$), and small intestinal surgery ($n=25$) were excluded from the study. Data were retrieved from prospectively maintained databases and included baseline patient characteristics (demographic data, preoperative risk factors, and comorbidities), operative characteristics, and postoperative outcomes. All operations were performed after obtaining informed consent from each patient. The local institutional review board approved this study (ID: 2013091712).

Indications of surgery

Surgical procedures were divided into three categories to assess the influence of each surgical procedure on the development of postoperative delirium: upper gastrointestinal surgery including esophagostomy and gastrectomy, colorectal surgery including colectomy and proctectomy, and

hepato-biliary-pancreatic surgery including hepatectomy, pancreatectomy, splenectomy, and cholecystolithotomy. Laparoscopic surgery was not used as an emergency procedure and in patients presenting with low cardiopulmonary function. As a history of previous operation was associated with worse surgical and postoperative outcomes after laparoscopic approach in our institution, these patients were basically excluded from the indication of laparoscopic approach.

Anesthesia

Epidural anesthesia was used in all patients unless specifically contraindicated. General anesthesia was used comprising administration of fentanyl, propofol, sevoflurane, rocuronium, and sugammadex without premedication.

Definition of postoperative delirium

Postoperative delirium was defined based on the Confusion Assessment Method criteria [14], which state that the diagnosis of delirium requires the presence of the following features: (1) an acute onset of cognitive impairment showing a fluctuating course and (2) at least two of the following: (a) perceptual disturbances, (b) a disorganized thought process, (c) disorientation and memory impairment, (d) an altered level of consciousness, and (e) hyper or hypoactive psychomotor activity. Abnormal behavior was defined as agitation, frequent summoning of nurses, removal of catheter lines, tubes, or dressings, and leaving the bed and wandering. Postoperative delirium was diagnosed and treated by both, surgeons and psychiatrists.

Variables studied

A performance status scale was used to assess functional status of patients. We defined comorbidity as follows: Cardiac disease was defined as the presence of at least one of the following diseases—coronary artery disease, heart failure, severe heart valve disease, myocardial disease, and arrhythmia. Pulmonary disease included the presence of at least one of the following diseases—asthma, chronic obstructive pulmonary disease, bronchiectasis, sequelae of pulmonary tuberculosis or tuberculous pleurisy, and interstitial lung disease. Cerebrovascular disease included the presence of at least one of the following conditions—intracerebral hemorrhage and cerebral infarction. Psychiatric disease included the presence of at least one of the following diseases—depression, manic depression, and schizophrenia. All patients were preoperatively evaluated by anesthesiologists and classified into six grades based on the American Society of Anesthesiologists (ASA) Physical Status classification system. Postoperative morbidity was graded based on the Clavien–Dindo classification [15], and according to this

grading, grade III, IV, and V complications were defined as “major.”

Statistical analyses

Continuous variables are expressed as a mean \pm standard deviation (SD) and were compared using the Student's *t* test. Categorical variables are expressed as a number (%) and were compared using the chi-squared test or the Fisher exact test. A Cox proportional hazard model analysis was performed to identify risk factors for the development of postoperative delirium or overall survival within 180 days after surgery, and factors showing $p < 0.05$ using univariable analyses were subjected to multivariable analysis. Operative time was divided by a mean value. The cut-off level to express estimated blood loss was set at 1000 mL [9] based on previous reports. Propensity score-matching analysis was used to develop a matched group of patients. The propensity score model was developed using a logistic regression model adjusting for incidence of diabetes mellitus, cardiac disease, pulmonary disease, cerebrovascular disease, concurrent malignant neoplasms, performance status ≥ 2 , ASA status ≥ 3 , upper gastrointestinal operations, hepato-biliary-pancreatic operations, and emergency operations. A 1:1 match without replacement was performed using logit (propensity score) through the nearest available matching with the caliper set at 0.05. After propensity score-matching, continuous and categorical variables were compared using the paired *t* test and McNemar test, respectively. Incidence of postoperative delirium was

assessed using the Kaplan–Meier method and compared using the log-rank test. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using JMP software (version 12.2.0; SAS Institute Inc., Cary, NC, USA).

Results

Patient demographics

We studied 530 men and 271 women with a mean age \pm SD of 68.7 ± 11.2 years. Operative procedures included upper gastrointestinal surgery in 300 (37.4%) patients, colorectal surgery in 332 (41.4%) patients, and hepato-biliary-pancreatic surgery in 169 (21.1%) patients. A laparoscopic approach and an open approach were used in 181 (22.6%, the laparoscopic group) patients and 620 (77.4%, the open group) patients, respectively. Baseline characteristics were compared between the laparoscopic and open groups (Table 1). Preoperative comorbidity rates were significantly lower in the laparoscopic group compared to the open group with regard to diabetes mellitus ($p = 0.035$), cardiac disease ($p = 0.005$), pulmonary disease ($p = 0.037$), and cerebrovascular disease ($p = 0.006$). Intra and postoperative outcomes are shown in Supplementary Table 1. The overall morbidity rate was 45.8% ($n = 367$) including postoperative delirium (7.0%, $n = 56$), and the major complication rate was 13.4% ($n = 108$).

Table 1 Baseline patient characteristics between the groups

Variables	All ($n = 801$)	Laparoscopic group ($n = 181$)	Open group ($n = 620$)	<i>p</i> value
Patient characteristics				
Men/women	530/271	109/72	421/199	0.055
Age (years)	68.7 ± 11.2	68.4 ± 10.6	68.8 ± 11.4	0.660
BMI (kg/m^2)	22.9 ± 3.6	23.2 ± 3.3	22.8 ± 3.7	0.239
Comorbidities				
Hypertension (%)	284 (35.5)	54 (29.8)	230 (37.1)	0.072
Diabetes mellitus (%)	203 (25.3)	35 (19.3)	168 (27.1)	0.035
Cardiac disease (%)	215 (26.8)	34 (18.8)	181 (29.2)	0.005
Pulmonary disease (%)	43 (5.4)	4 (2.2)	39 (6.3)	0.037
Cerebrovascular disease (%)	76 (9.5)	8 (4.4)	68 (11.0)	0.006
Dementia (%)	5 (0.6)	0 (0)	5 (0.8)	0.593
Psychiatric disease (%)	23 (2.9)	3 (1.7)	20 (3.2)	0.323
Concurrent malignant neoplasm (%)	683 (85.3)	171 (94.5)	512 (82.6)	$< .001$
Performance status ≥ 2 (%)	37 (4.6)	2 (1.1)	35 (5.7)	0.008
ASA status ≥ 3 (%)	116 (14.5)	10 (5.5)	106 (17.1)	$< .001$

ASA the American Society of Anesthesiologists Physical Status classification system, BMI body mass index, PS performance status

Risk factors associated with the development of postoperative delirium

Univariable analyses showed age ≥ 65 years, history of psychiatric disease, performance status ≥ 2 , ASA status ≥ 3 , a laparoscopic approach, emergency surgery, and postoperative ICU stay were significantly associated with postoperative delirium. Subsequent analysis performed using the Cox proportional hazards model revealed that a laparoscopic approach was associated with a lower risk of development of postoperative delirium [hazard ratio (HR) 0.30, 95% confidence interval (CI) 0.07–0.84, $p=0.019$]. In contrast, age ≥ 65 years (HR 3.32, 95% CI 1.49–8.83, $p=0.002$), history of psychiatric disease (HR 3.23, 95% CI 1.17–7.51, $p=0.026$), and performance status ≥ 2 (HR 2.50, 95% CI 1.08–5.28, $p=0.033$) were shown to be independent risk factors associated with the development of postoperative delirium (Table 2).

Risk of postoperative delirium on overall survival within 180 days after surgery

Onset of postoperative delirium was 2.6 ± 3.8 days (median [range], 1 [0–19] days) postoperatively and its duration was 12.2 ± 23.9 days (median [range], 5 [1–150] days). Comparison of postoperative outcomes between patients with and

without postoperative delirium is summarized in Supplementary Table 2. The length of postoperative hospitalization was significantly longer in patients with postoperative delirium compared to those without postoperative delirium. We found that postoperative delirium was associated with a higher risk of overall survival within 180 days (HR 4.91, 95% CI 1.96–12.22, $p=0.001$) after adjusting for other confounders using the Cox proportional hazard model analysis (Supplementary Table 3).

Evaluation of the incidence of delirium using propensity score-matching analysis

After 1:1 case propensity score-matching, 181 patients in the laparoscopic group and 181 patients in the open group were analyzed. Patient demographics were found to be comparable after the matching was performed (Table 3). The amount of estimated blood loss was lower in the laparoscopic group than in the open group (Table 4). Cumulative incidence rates of postoperative delirium were significantly lower in the laparoscopic group compared to the open group (30-day cumulative incidence rate, 1.7% vs. 7.8%, $p=0.006$) (Fig. 1). The rates of morbidity except delirium, major complication, and hospital mortality were significantly lower in the laparoscopic group than in the open group.

Table 2 Assessment of risk factors associated with postoperative delirium using Cox proportional hazards model analysis

Variables	Univariable analysis			Multivariable analysis		
	HR	95% CI	<i>p</i> value	HR	95% CI	<i>p</i> value
Sex (men/women)	1.35	0.75–2.59	0.327			
Age (≥ 65 / < 65 years)	3.96	1.83–10.34	$<.001$	3.32	1.49–8.83	0.002
Comorbidities						
Hypertension	0.90	0.49–1.58	0.708			
Diabetes mellitus	1.10	0.58–2.00	0.754			
Cardiac disease	1.14	0.60–2.04	0.676			
Cerebrovascular disease	1.84	0.80–3.71	0.138			
Dementia	3.22	0.18–14.67	0.330			
Psychiatric disease	4.75	1.81–10.29	0.003	3.23	1.17–7.51	0.026
Concurrent malignant neoplasms	0.80	0.41–1.75	0.552			
Performance status ≥ 2	5.39	2.55–10.34	$<.001$	2.50	1.08–5.28	0.033
ASA status ≥ 3	3.02	1.65–5.33	$<.001$	1.71	0.86–3.25	0.124
Surgical factors						
Operation time (≥ 306 / < 306 min)	0.96	0.51–1.59	0.889	1.17	0.60–2.23	0.638
Blood loss (≥ 1000 / < 1000 mL)	0.59	0.30–1.30	0.176	0.98	0.46–2.30	0.964
Type of surgery						
Colorectal	1.00 (reference)	–	–			
Upper gastrointestinal	1.50	0.80–2.87	0.206			
Hepato-biliary-pancreatic	1.48	0.69–3.08	0.302			
Laparoscopic approach	0.22	0.05–0.59	0.001	0.30	0.07–0.84	0.019
Emergency surgery	2.44	1.91–6.81	0.028	0.99	0.38–2.34	0.992
Postoperative ICU stay	4.73	2.46–8.57	$<.001$	2.24	0.98–4.79	0.055

Table 3 Comparison of patient demographics between the groups after propensity score-matching

Variables	Laparoscopic group (n = 181)	Open group (n = 181)	p value
Patient characteristics			
Men/women	109/72	123/58	0.122
Age (in years)	68.4 ± 10.6	67.8 ± 10.7	0.288
BMI (kg/m ²)	23.2 ± 3.3	22.2 ± 3.8	0.117
Comorbidities			
Hypertension (%)	54 (29.8)	46 (25.4)	0.285
Diabetes mellitus (%)	35 (19.3)	32 (17.7)	0.083
Cardiac disease (%)	34 (18.8)	34 (18.8)	> .999
Pulmonary disease (%)	4 (2.2)	4 (2.2)	> .999
Cerebrovascular disease (%)	8 (4.4)	6 (3.3)	0.157
Dementia (%)	0 (0)	1 (0.6)	0.317
Psychiatric disease (%)	3 (1.7)	8 (4.4)	0.132
Concurrent malignant neoplasms (%)	171 (94.5)	170 (93.9)	0.564
Performance status ≥ 2 (%)	2 (1.1)	2 (1.1)	> .999
ASA status ≥ 3 (%)	10 (5.5)	12 (6.6)	0.157

ASA, the American Society of Anesthesiologists Physical Status classification system, BMI body mass index, PS performance status

Table 4 Comparison of intra- and postoperative outcomes between the groups after propensity score-matching

Variables	Laparoscopic group (n = 181)	Open group (n = 181)	p value
Operation type			
Upper gastrointestinal ^a (%)	103 (56.9)	103 (56.9)	> .999
Colorectal ^b (%)	65 (35.9)	66 (36.5)	0.564
Hepato-biliary-pancreatic ^c (%)	13 (7.2)	12 (6.6)	0.317
Emergency surgery (%)	0	0	–
Intraoperative outcomes			
Operation time (min)	310.5 ± 115.1	309.9 ± 133.9	0.991
Intraoperative bleeding (mL)			
Mean ± SD	87.1 ± 187.7	460.6 ± 738.0	< .001
Median (range)	21.0 (0–1692.0)	290.0 (0–8050.0)	< .001*
Red blood cell transfusion (%)	1 (0.6)	32 (17.7)	< .001
Postoperative outcomes			
Postoperative ICU stay (%)	5 (2.8)	15 (8.3)	0.018
Postoperative delirium (%)	3 (1.7)	10 (5.5)	0.002
Morbidity except delirium (%)	42 (23.2)	75 (41.4)	< .001
Major complications (%)	13 (7.2)	25 (13.8)	0.040
Hospital mortality (%)	0	5 (2.8)	0.025
Length of hospitalization (days)			
Mean ± SD	11.8 ± 21.1	17.3 ± 22.1	0.016
Median (range)	6.0 (4.0–182.0)	10.0 (0–234.0)	< .001*
Post-discharge institutionalization (%)	3 (1.7)	17 (9.4)	0.012

ICU intensive care unit

*Wilcoxon rank-sum test

^aEsophagostomy and gastrectomy

^bColectomy and proctectomy

^cHepatectomy, pancreatectomy, splenectomy, open cholecystectomy, and cholecystolithotomy

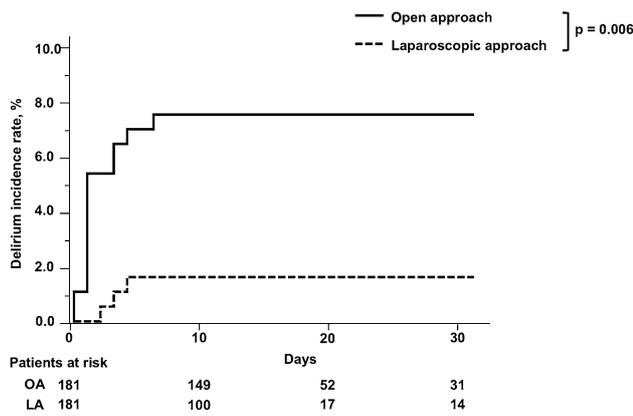


Fig. 1 Incidence of postoperative delirium stratified based on a laparoscopic and open approach after propensity score-matching. LA laparoscopic approach, OA open approach

Discussion

The present study demonstrated that the incidence of postoperative delirium after major abdominal surgery was significantly lower in the laparoscopic group compared to the open group for both, unmatched and matched cohorts. A Multivariable Cox proportional hazard model analysis revealed that a laparoscopic approach was associated with a lower risk of postoperative delirium in patients undergoing major abdominal surgery.

A laparoscopic approach was reportedly shown to reduce the period of hospitalization [16] and postoperative complications including prolonged ileus [17, 18], wound infection [12], and postoperative pneumonia [13]. However, the association between a laparoscopic approach and the development of postoperative delirium remains unclear. A laparoscopic approach was reported not to reduce the incidence of postoperative delirium in elderly patients undergoing gastrectomy [19]. Our study showed that a laparoscopic approach reduced the risk of postoperative delirium which was associated with poor short- and long-term outcomes. The poor outcomes in patients with postoperative delirium are in line with previous reports [2, 4–6], and postoperative delirium should be prevented.

Pathophysiology of postoperative delirium is multifactorial in nature in that this condition occurs as a consequence of a complex interrelationship between predisposing and precipitating factors [20–22]. With respect to our study, age ≥ 65 years, history of psychiatric disease, and a performance status ≥ 2 were found to be independent risk factors associated with the development of postoperative delirium, which was consistent with results obtained from previous studies [2, 5–7]. A laparoscopic approach was found to be an independent factor associated with a 0.30-fold lower risk of postoperative delirium. Similarly, cumulative incidence rates of postoperative delirium

were significantly lower in the laparoscopic group compared to the open group after propensity score-matching. The most likely explanation for this finding is that compared to open surgery, a laparoscopic approach successfully suppresses the systemic stress and inflammatory response occurring in relation to surgical procedures [23, 24]. This theory is supported by recent reports revealing that a systemic inflammatory response is associated with the pathogenesis of delirium [25, 26] and that levels of inflammatory cytokines including C-reactive protein, interleukin-6, interleukin-8, and interleukin-10 after surgery for management of hip fracture were found to be higher in mentally impaired patients compared to cognitively normal patients [25]. The high interleukin-6 and cortisol concentrations observed after cardiac surgery are associated with a higher incidence of postoperative delirium [26].

Limitations of our study

1. Ours was a retrospective study and complete adjustments for all confounders were not possible despite the use of a multivariable Cox proportional hazard model analysis and propensity score-matching analysis. In particular, it should be noted that laparoscopic surgery was not used as an emergency procedure and in patients presenting with previous history of operations and low cardiopulmonary function. Laparoscopic pancreaticoduodenectomy was not performed because the national insurance system did not cover the procedure during the study period.
2. The association between postoperative delirium and other reported risk factors including cognitive function before and after surgery and a previous episode of postoperative delirium were not assessed because these data were not available in our study.

In conclusion, a laparoscopic approach used to perform major abdominal surgeries reduced a risk of postoperative delirium, which was associated with a longer postoperative hospitalization, higher post-discharge institutionalization, and a higher risk of overall survival within 180 days after surgery.

Compliance with ethical standards

Disclosures Drs. Kyoji Ito, Yusuke Suka, Motoki Nagai, Keishi Kawasaki, Mariko Yamamoto, Daisuke Koike, Yukihiro Nomura, Nobutaka Tanaka, Yoshikuni Kawaguchi have no conflicts of interest or financial ties to disclose.

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