

Factors affecting the onset of hyperactive delirium following surgery for gastrointestinal cancer

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I. Introduction

Surgery is a physically invasive procedure that results in tissue damage and the loss of organs or tissue as well as blood and other bodily fluids. Biological reactions, including neuroendocrine and inflammatory reactions, are evoked during the process of recovery from this invasion, causing a range of physical and psychological symptoms. Although these postoperative biological reactions are physiological phenomena, when they exceed their normal bounds they are regarded as complications that impair systemic function, including the respiratory, circulatory, digestive, and urological systems, and may even put the patient's life at risk.

Postoperative delirium reportedly occurs as a general postoperative complication in approximately 5% of patients.¹⁾ Although postoperative delirium itself poses no risk to survival, the hallucinations, delusions, restlessness, agitation, and disorientation displayed by patients with hyperactive delirium (in this paper, "delirium" refers only to hyperactive delirium) may cause them to remove intravenous lines, drains, and tubes necessary for postoperative systemic management, or make them fall after inappropriately trying to get out of bed. As a result, they may hurt themselves, reduce the effectiveness of treatment, or increase their risk for postoperative complications. All of these possibilities create difficulties in postoperative management that have implications in a range of different areas, including increased mortality, longer hospital length of stay,^{2, 3)} and a heavier burden on families.

Factors causing delirium include predisposing factors such as old age and declining brain function, initiating factors such as stress and sleep disturbance due to change of environment that promote the onset of delirium, and direct factors such as a history of central nervous system disorders or metabolic disorders that affect brain function.⁴⁾ Postoperative delirium is directly related to surgical invasion. Preoperative factors that have been identified as contributing to the onset of delirium include old age, dementia, physical complications, and a history of smoking.²⁾ Intraoperative factors include amount of hemorrhage⁵⁾ and operative time.⁶⁾ Postoperative factors include difficulty in controlling pain, hypotension, anemia, and fever.^{5, 7)} In addition to these physical causes, environmental causes have also been suggested, including the sense of isolation, few visits, and physical restraints imposed on patients admitted to the postoperative intensive care unit (ICU).⁸⁾

The reported incidence of delirium varies widely between studies according to the definition of delirium used and the characteristics of study subjects. Numerous reports have pointed out that the incidence of postoperative delirium is high following gastrointestinal surgery. The reason for the higher incidence of delirium following gastrointestinal surgery is unclear, but possible causes may include the fact that patients undergoing gastrointestinal surgery have risk factors for delirium including nutritional disturbance⁹⁾ and severe postoperative pain.

Because delirium has multiple causes, its prediction and diagnosis are problematic. The condition of delirium is a temporary symptom; therefore, it cannot be dealt with proactively.¹⁰⁾ Following gastrointestinal

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surgery, which involves the insertion of a large number of drains and tubes, delirium-related incidents pose a particular risk because they may affect the patient's prognosis. In this study, we demonstrated that the onset of delirium in patients who underwent surgery for gastrointestinal cancer differed according to surgical procedure, age, type of disorder, and duration of anesthesia.

II. Objective

The objective of this study was to elucidate factors affecting the onset of delirium in patients who had undergone surgery for gastrointestinal cancer, with the goal of providing a basic resource for the prevention of delirium and delirium-related incidents.

III. Methods

1. Subjects

We reviewed the clinical records (electronic medical records) of 348 patients who underwent surgery under general anesthesia in the gastrointestinal surgery ward of a university hospital between the 2004 and 2008 academic years.

2. Research period

The project was conducted between June 2009 and December 2009.

3. Study methods

We performed a retrospective study based on data contained in each patient's electronic medical record. The data gathered included age, sex, type of disorder, type of surgical procedure, duration of anesthesia, and inserted devices (drains, tubes, etc.), as well as whether symptoms of delirium were present between the day of surgery and the sixth postoperative day. Delirium symptoms were defined in terms of the DSM-IV diagnostic criteria for delirium,¹¹⁾ with disturbance of consciousness, attention, cognition, or perception as obligatory symptoms. Because hypoactive delirium is difficult to differentiate from other physical symptoms, in this study we focused on active delirium, and identified patients who developed delirium as those whose recorded symptoms included visual or auditory hallucinations, strange behavior, disorientation, agitation, or wandering.

4. Analytical methods

SPSS Statistics 16.0 (IBM Company, USA) was used for analysis. Descriptive statistics and frequency distribution were obtained on attributes of subjects. The subjects were categorized into two groups, a delirium group and a non-delirium group, depending on whether the patients had exhibited delirium. The two groups were compared by sex, age (≥ 65 years, ≤ 64 years), type of disorder, and surgical category (elective/emergency surgery) by using a χ^2 test, and the incidence of delirium for each attribute was calculated. A t-test was used for mean age of subject at the time of onset of delirium and mean duration of anesthesia. The level of statistical significance was set at 5%.

5. Ethical considerations

This study was approved by the department of Nursing, Nagoya City University Hospital. No information that would identify individuals was taken from the electronic medical records when data were gathered, and the computer into which the data were input was kept isolated from networks, with external memory devices stored strictly under lock and key.

IV. Results

1. Attributes

In terms of patient characteristics, the study subjects comprised 220 men (63.2%) and 128 women (36.8%), with a mean age of 66.3 ± 12.0 years. The main disorders were colorectal cancer (44.3%), gastric cancer (26.7%), esophageal cancer (10.1%), pancreatic cancer (10.1%), liver cancer (6.9%), and gallbladder cancer (2.0%) (Table 1). The main surgical procedures were colectomy, gastrectomy, cholecystectomy, esophagectomy, pancreatectomy, and hepatectomy. Of these procedures, 85.9% were performed via laparotomy (open surgery) and 13.5% laparoscopically. In terms of surgical category, 96.8% of the procedures were elective surgery and 3.2% were emergency surgery. The mean age of the patients who underwent emergency surgery was 72.1 ± 13.2 years, higher than the mean age of those who underwent elective surgery at 66.1 ± 11.9 years, but the difference was not significant. The mean duration of anesthesia was 324.6 ± 141.4 minutes (minimum, 64 minutes; maximum, 784 minutes). The mean duration of anesthesia was 324.0 ± 142.0 minutes for open surgery and 337.4 ± 133.3 minutes for laparoscopic surgery.

The maximum total number of IV injection routes, oxygen tubes, bladder catheters, and drains placed in patients postoperatively (maximum number of insertions) was 6 in 22.4% of the patients, the highest proportion of patients, followed by 7 in 20.7%, 8 in 13.2%, and 5 in 12.6%, with a mean 6.8 ± 2.1 insertions (minimum, 2; maximum, 13). Table 2 shows the maximum number of insertions by disorder. A somewhat higher number of insertions was used in patients with esophageal or pancreatic cancer.

2. Breakdown of delirium symptoms (total numbers)

The most commonly identified symptom of delirium was strange behavior (68 patients), followed by hallucinations (36 patients), disorientation (35 patients), agitation (21 patients), wandering (11 patients), and auditory hallucinations (1 patient).

3. Incidence of delirium

Delirium occurred in 66 patients (19.0%). The incidence of delirium among all subjects was 3.7% on the day of surgery, increasing to a peak of 4.9% on the first and second postoperative days, then declining to 3.2% on the third postoperative day, 1.4% on the fourth, 0.6% on the fifth, and 0.3% on the sixth. Symptoms initially appeared on the first or second postoperative day in 25.8% of the 66 patients who exhibited delirium. Delirium continued for a mean of 1.9 ± 1.2 days (minimum 1, maximum 7), with symptoms resolving within a day in 47.7% of patients. The incidence was significantly higher among men at 22.3%, compared with 13.3% among women ($p = 0.047$). By disorder, the incidence of delirium was 28.6% for gallbladder cancer, 25.7% for pancreatic cancer, 22.9% for esophageal cancer, 18.8% for colorectal cancer, 16.1% for gastric cancer, and 12.5% for liver cancer.

The mean age of the delirium group was 74.1 ± 10.0 years, significantly higher than that of the non-

Table 1 Characteristics of the Study Subjects

No. of subjects		348
Age (years)		66.3 ± 12.0
Sex	male	220 (63.2%)
	female	128 (36.8%)
Main disorders	esophageal cancer	35 (10.1%)
	gastric cancer	93 (26.7%)
	colorectal cancer	154 (44.3%)
	pancreatic cancer	35 (10.1%)
	liver cancer	24 (6.9%)
	gallbladder cancer	7 (2.0%)
procedures	open surgery	299 (85.9%)
	laparoscopically	47 (13.5%)
	others	2 (0.6%)
surgical category	elective	337 (96.8%)
	emergency	11 (3.2%)

Table 2 The number of insertions

Main disorders	Mean \pm SD	Minimum to maximum
esophageal cancer	9.2 ± 2.8	2–13
gastric cancer	6.8 ± 1.5	4–12
colorectal cancer	5.7 ± 1.6	2–11
pancreatic cancer	8.6 ± 1.6	6–12
liver cancer	7.3 ± 1.0	5–9
gallbladder cancer	6.1 ± 2.9	2–10

delirium group (64.4 ± 11.7 years; $p=0.000$). There was a weak correlation between age and delirium onset ($r=0.238$); the incidence of delirium among patients aged 65 years was 26.7%, significantly higher than that among patients aged 64 years (7.7%; $p=0.000$). In terms of age group, patients aged 65 accounted for 83.3% of those who exhibited symptoms of delirium. All 3 patients who had been diagnosed preoperatively with dementia (2 patients with colorectal cancer, 1 patient with gallbladder cancer) developed delirium between the first and third postoperative days, and the delirium continued for a mean of 3 days. By surgical procedure, the incidence of delirium was 20.7% after open surgery, significantly higher than the 8.5% after laparoscopic surgery ($p=0.030$). Patients who underwent open surgery accounted for the great majority of cases of delirium at 93.9%, with only 6.1% of the patients who experienced delirium having undergone laparoscopic surgery. In terms of surgical category, the incidence of delirium after elective surgery was 18.1%, significantly lower than the 45.5% incidence of delirium after emergency surgery ($p=0.038$).

The incidence of delirium was 0% when the duration of anesthesia was 120 minutes and approximately 15-18% for 121-479 minutes; however, the incidence rose to 28.2% for anesthesia duration of 480-599 minutes and 37.5% for anesthesia duration of 600-719 minutes. The mean duration of anesthesia was around 40 minutes longer in the delirium group, at 356.6 ± 160.9 minutes, compared with 317.0 ± 135.7 minutes in the non-delirium group. This difference was significant ($p=0.041$).

The mean maximum number of devices inserted in patients in the delirium group was 6.9 ± 2.3 , and the mean number in the non-delirium group was 6.8 ± 2.0 , with no significant difference between the groups. In terms of maximum number of insertions, a comparison of the incidence of delirium among those patients with more (≥ 7) or less (≤ 6) than the median number of inserted devices showed that delirium occurred among 18.1% of patients with ≥ 7 insertions (182 patients) and 19.9% of those with ≤ 6 insertions (166 patients), with no significant difference between the two groups.

V. Discussion

The incidence of delirium is reportedly high among elderly people.⁴⁾ The present study also found that the onset of postoperative delirium is associated with old age. The psychological characteristics of elderly people include such mental problems as the experience of loss or some form of anxiety, as well as declining cognitive functions due to aging. All of this can result in the inability of elderly people to properly recognize their symptoms or adjust to a change in their environment due to hospitalization.⁷⁾ Many elderly people also suffer from underlying conditions, meaning that multiple causes may increase the incidence of delirium.

Delirium is also known to be more common among men.⁷⁾ The reason for this is unclear, but it has been pointed out that factors that worsen atherosclerotic vascular lesions, such as smoking and drinking alcohol, are more common in men, and this may be related to their higher rate of delirium.¹²⁾ The higher rate of delirium in men may also be affected by the higher incidence of gastrointestinal cancer among men compared with women.

Possible reasons for the higher incidence of delirium following surgery for esophageal cancer and pancreatic cancer may include the high degree of surgical invasiveness compared with other gastrointestinal surgical procedures, meaning that postoperative pain, fever, and hematological abnormalities are more likely to occur. Malnutrition due to reduced food intake preoperatively is also frequent, and there is a high likelihood of patients' conditions causing electrolyte imbalances or malnutrition. The long postoperative fasting period is also a factor that encourages patients' nutritional state to worsen. Not eating also changes the rhythm of patients' daily lives, potentially destroying their circadian rhythm and modulating their sleeping patterns. In addition, the laryngeal and tracheal resection, esophageal reconstruction, and widespread lymph node dissection involved in esophageal cancer surgery result in surgical wounds to the

neck, chest, and abdomen, while the large incision required for pancreatic surgery also results in intense postoperative pain at the wound site. All of this may affect the onset of delirium.

Several peritoneal drains are normally inserted after open gastrointestinal surgery. Although our study results did not provide conclusive evidence that the number of devices inserted affects the incidence of delirium, the presence of such inserted devices as IV lines and drains tends to restrict bodily movements and produce discomfort on moving, as well as cause patients to be fearful of accidentally removing the devices. It is possible that these feelings of confinement may lead to delirium. Esophageal cancer surgery involves thoracotomy, requiring the insertion of several chest drains. Pancreatic surgery requires pancreatic duct and bile duct drains, meaning that the number of insertions is larger compared with other types of gastrointestinal surgery. It has previously been reported that the incidence of delirium is higher in patients who have undergone gastrointestinal or general surgery in whom ≥ 6 devices have been inserted. The high number of insertions is probably one factor in the high incidence of delirium following esophageal and pancreatic surgery.

In terms of surgical procedures, the present study found the incidence of delirium to be higher after open surgery compared with laparoscopic surgery. There was found no difference in the duration of anesthesia between these types of procedures; the difference is conjectured to lie in their levels of surgical invasiveness. Laparoscopic surgery generally involves a small surgical wound and little postoperative pain, enabling patients to get up soon after surgery and to recover quickly. Open surgery involves a large wound and intense postoperative pain, together with the insertion of drains; it can be conjectured that this is the reason for the higher incidence of delirium after open surgery.

Previous studies have found no difference between emergency and elective surgery with respect to the occurrence of delirium,¹³⁾ however, the present study found the incidence to be higher after emergency surgery. Emergency gastrointestinal surgery is frequently performed to treat ileus or peritonitis due to gastric or intestinal perforation. In many cases, preoperative deterioration of the patient's systemic condition is already evident due to an underlying malignant gastric or colorectal cancer, or patients may already exhibit electrolyte imbalances or hematological abnormalities that are regarded as direct causes of delirium. In almost all cases, emergency surgery is performed without time to correct these imbalances, causing patients to be physically unprepared for the rigors of surgery. In addition, emergency surgery cannot generally be preceded by adequate patient education or orientation to the upcoming procedure. The urgent nature of emergency surgery means that in many cases it is not possible to take preparatory measures to reduce initiating factors for delirium such as change of environment and psychological stress; patients undergoing emergency surgery therefore tend to be psychologically unprepared compared with those undergoing elective surgery. Opinion is divided on the association between preoperative anxiety and delirium, with some studies finding an association¹⁴⁾ and other studies ruling it out.¹⁵⁾ Nevertheless, an understanding of the psychological issues involved is necessary to analyze the characteristics of patients undergoing emergency surgery.

Postoperative delirium is said to occur most frequently on the second and third postoperative days and to occur up to the fourth or fifth postoperative day. Our study results also found that the onset of delirium peaked on the second postoperative day. Hematological abnormalities and electrolyte imbalances tend to occur during the period beginning immediately after surgery until the second postoperative day, and pain is also most intense during this period. This raises the possibility that the sleep/wake cycle will be disrupted. Feelings of confinement, stress due to pain, and restrictions on movement because of inserted devices may also be involved. This indicates that in addition to the current methods for helping patients sleep at night and effectively controlling their pain, it is also important to minimize patients' sense of confinement. Additionally, it is necessary to be aware that the mere presence of inserted IV lines, drains, and other devices may pose a risk for delirium in itself, regardless of the number of insertions. The inserted devices should be organized to allow as much freedom of movement as possible, and should be removed

swiftly at the appropriate time.

Although delirium is regarded as difficult to prevent, it is important to perform a risk assessment for delirium by gathering such information as the patient's age, type of surgical procedure, anxiety level, general preoperative condition, and intensity of postoperative pain.¹⁶⁾ Should delirium occur, the response should include eliminating its cause, controlling its symptoms, providing nursing care to help the patient remain oriented or recover from disorientation, and taking measures to ensure patient safety. These actions are required in parallel with treatment to restore the patient's general condition.

VI. Study limitations

Numerical bias was present with respect to the disorders suffered by the subjects of this study and the type of surgery indicated. Because we did not investigate other patient characteristics, such as general preoperative condition and the occurrence of complications, it was not possible to calculate the risk of delirium accurately from patient attributes. We were therefore limited to indicating trends. Because this was a retrospective study for which the data were obtained from electronic medical records, it must be acknowledged that the content as recorded in the electronic medical records was inconsistent between different recorders, and that our study therefore lacked accuracy.

VII. Conclusion

We carried out a retrospective survey of the circumstances surrounding the onset of postoperative delirium from the content of medical records of 348 patients who underwent surgery for gastrointestinal cancer. In terms of type of disorder, postoperative delirium occurred more frequently after surgery for gallbladder, pancreatic, and esophageal cancer. Patient age, type of surgical procedure, time elapsed after surgery, and inserted devices were also conjectured to affect delirium. Delirium tended to occur more frequently in relation to the following factors: male sex, age ≥ 65 years, open surgery or emergency surgery, long duration of anesthesia, and second postoperative day. Patients with these factors should be regarded as having high risk for the development of postoperative delirium and requiring preoperative intervention to help prevent its onset.

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