

## Psychological Risk Factor of Postoperative Delirium in Patients with Gastrointestinal Cancer

Yusuke OCHIAI, Akihisa KOBORI, Kazutaka NUKARIYA, and Kazuhiko NAKAYAMA

*Department of Psychiatry, The Jikei University School of Medicine*

### ABSTRACT

**Purpose :** To determine whether some patients are at high risk for postoperative delirium, we investigated psychological risk factors in patients awaiting surgery for gastric or colorectal cancer.

**Methods :** Patients with gastric or colorectal cancer who were 65 years or older and had been admitted to The Jikei University Kashiwa Hospital underwent the following tests before surgery : the Hospital Anxiety and Depression Scale (HADS), the 28-item version of the General Health Questionnaire (GHQ-28), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), and the Mental Adjustment to Cancer scale (MAC scale). During a 7-day postoperative observation period, delirium was diagnosed, if present, with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, and the Confusion Assessment Method for the Intensive Care Unit.

**Results :** Postoperative delirium was diagnosed in 17 (15.6%) of 109 patients. Compared with other patients, these patients had significantly higher scores for Anxiety (HADS), total score (GHQ-28), Appetite loss (EORTC QLQ-C30) and Helplessness/Hopelessness (MAC scale) and significantly lower scores for Role (EORTC QLQ-C30) and Fighting Spirit (MAC scale). These patients also had a significantly higher Helplessness/Hopelessness score (odds ratio = 1.356 ; 95% confidence interval = 1.082-1.698 ;  $p < 0.01$ ).

**Conclusions :** This study has shown that patients who have strong helplessness and hopelessness before surgery are at a high risk for postoperative delirium. (Jikeikai Med J 2016 ; 63 : 37-43)

**Key words :** delirium, postoperative delirium, risk factor, gastric cancer, colorectal cancer

### INTRODUCTION

Delirium is a state of acute brain dysfunction based on a disorder of consciousness. Delirium is often accompanied by cognitive dysfunction, but acutely developing circadian variation stands out, and its chance of reversibility is often different from that of dementia. Many cases of postoperative delirium are reported to appear within 3 to 4 days after surgery<sup>1,2</sup>.

Risk factors for delirium have been classification by Lipowski<sup>3</sup> as predisposing factors, precipitating factors, and facilitating factors. As a facilitating factor for delirium, psychological stress has been classified ; however, what specific types of stress act as risk factors is unclear. Most studies of the risk factors of postoperative delirium have eliminated age and physical complications<sup>4-7</sup>, but several studies have examined the relationship between postoperative delirium and various psychological conditions<sup>8,9</sup>. There-

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落合 結介, 小堀 聡久, 忽滑谷和孝, 中山 和彦

Mailing address : Yusuke OCHIAI, Department of Psychiatry, The Jikei University Kashiwa Hospital, 163-1 Kashiwashita, Kashiwa-shi, Chiba 277-8567, Japan.

E-mail : persona@jikei.ac.jp

fore, to determine whether some patients are at greater risk for postoperative delirium, in the present study we assessed the psychological state with multiple psychological tests in patients awaiting surgery for gastric or colorectal cancer and assessed the incidence of postoperative delirium with a follow-up survey.

## METHODS

### *Subjects*

The subjects were patients who had been admitted to The Jikei University Kashiwa Hospital to undergo elective surgery for gastric or colorectal cancer. Patients who met all of the following criteria were selected as subjects: 65 years or older; primary cancer of the stomach or colon; stages 1 to 3 according to the Union for International Cancer Control Staging System, Seventh Edition<sup>10</sup>; no history of organic brain disease; no use of psychotropic medication; a performance status of 0 to 3 on the Eastern Cooperative Oncology Group scale<sup>11</sup>; no admission to the intensive care unit after surgery; and written, informed consent obtained after satisfactorily understanding the research contents.

This study was performed with the approval of the Ethics Committee of The Jikei University School of Medicine. The personal information of subjects was handled according to strict data-management protocols. Furthermore, written consent was obtained from all subjects to publish the results of this study.

### *Background factors*

The following factors were selected because they are considered to be conventional risk factors for delirium. Preoperative factors included age, sex, surgical site (stomach or colon), medical history (i.e., “yes” or “no” for hypertension, diabetes, coronary artery disease, lung disease, liver disease, and renal disease), drinking history (“yes” or “no”), and smoking history (“yes” or “no”). Intraoperative and postoperative factors included the type of surgery (laparotomy or laparoscopy), operation time, anesthesia time, volume of blood loss, need for blood transfusion, and blood-test findings on the day after surgery (albumin, calcium, and C-reactive protein levels).

### *Psychological tests*

Before surgery the subjects underwent 4 psychological

tests with self-reported questionnaire forms. The forms were distributed to subjects, filled out by them, and collected from them 1 or 2 days before surgery. Any order and length of time for answering the questionnaires was acceptable. The psychological tests and the states they were used to assess were as follows: the Hospital Anxiety and Depression Scale (HADS)<sup>12</sup>, anxiety and depression; the 28-item version of the General Health Questionnaire (GHQ-28)<sup>13,14</sup>, mental health; the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30)<sup>15</sup>, quality of life; and the Mental Adjustment to Cancer scale (MAC scale)<sup>16</sup>, psychological adjustment to cancer.

The MAC scale is a self-reported 40-item questionnaire for measuring the psychological adjustment of patients who have cancer. Question items are further categorized into 5 subscales: Fighting Spirit (16 items), Helplessness/Hopelessness (6 items), Anxious Preoccupation (9 items), Fatalism (8 items), and Avoidance (1 item). Higher scores in a given subscale signify that a corresponding psychological response is more strongly exhibited. For example, a higher Helplessness/Hopelessness score, with a total range of 6 to 24 points, indicates strengthened feelings of despair and powerlessness; in contrast, a higher Fighting Spirit score, with a total range of 16 to 64 points, indicates greater positivity and affirmation.

### *Assessment of postoperative delirium*

The observation period was the 7 days after surgery. Postoperative delirium, if present, was diagnosed with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision<sup>17</sup>, and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)<sup>18,19</sup>.

The CAM-ICU was developed to assess delirium among all patients, even those who cannot easily communicate verbally (e.g., those being treated with a ventilator). In the CAM-ICU protocol, the sedation and agitation levels of patients are first evaluated with the Richmond Agitation-Sedation Scale. Next, delirium is given a positive or negative diagnosis according to assessments in 4 categories: acute change or fluctuating course of mental status, inattention, altered level of consciousness, and disorganized thinking. The CAM-ICU can be performed in approximately 5 minutes and, according to a study of nurses who received standardized training used this method to assess delirium,

has a diagnostic sensitivity of 93% to 100% and a specificity of 98% to 100%<sup>19</sup>.

For analysis, variables were compared between patients in whom postoperative delirium had been or had not been diagnosed during the 7-day observation period.

#### Statistical analysis

The Mann-Whitney U test was used to compare each continuous variable and Fisher's exact test was used to compare each categorical variable between patients who had postoperative delirium and those who did not. Comparisons achieving  $P < 0.05$  were considered significant; items for which significant differences were observed in the univariate analysis were then subjected to logistic regression analysis. The software program IBM SPSS Statistics 16.0J for Windows (IBM Japan Ltd., Tokyo, Japan) was used for all statistical analyses.

## RESULTS

#### The incidence of postoperative delirium

In the 2 years from December 1, 2011, to November 30, 2013, 123 patients fulfilled the inclusion criteria for this study. Of these patients, 14 were excluded as subjects: 5

had incomplete responses on psychological tests, 7 had entered the intensive care unit after surgery, 1 had missing values in blood-test data, and 1 died in the hospital. The remaining 109 patients (88.6%) were subjects for analysis.

Postoperative delirium was diagnosed in 17 (15.6%) of these 109 patients. Because postoperative delirium is transient, it was not present in any of the 17 patients when they were discharged.

#### Preoperative, intraoperative, and postoperative factors

Preoperative factors (Table 1), intraoperative factors (Table 2), and postoperative factors (Table 2) did not differ significantly between patients who had or did not have postoperative delirium.

#### Psychological tests

The Anxiety score (HADS), total score (GHQ-28), Appetite loss score (EORTC QLQ-C30), and Helplessness/Hopelessness score (MAC scale) were significantly higher in patients who had postoperative delirium than in those who did not. In contrast, the Role score (EORTC QLQ-C30) and Fighting Spirit score (MAC scale) were significantly lower in patients who had postoperative delirium than in those who did not (Table 3).

Table 1. Preoperative factors of the patients

	Patients with postoperative delirium ( <i>n</i> = 17)	Patients without postoperative delirium ( <i>n</i> = 92)	<i>P</i> -value
Age (years)*	76.3 ± 6.5	73.9 ± 5.7	n.s. <sup>a</sup>
Sex			n.s. <sup>b</sup>
Female	3 (18%)	25 (27%)	
Male	14 (82%)	67 (73%)	
Surgical site			n.s. <sup>b</sup>
Stomach	10 (59%)	41 (45%)	
Colon	7 (41%)	51 (55%)	
Medical history			
Hypertension	10 (59%)	42 (46%)	n.s. <sup>b</sup>
Diabetes	3 (18%)	24 (26%)	n.s. <sup>b</sup>
Coronary artery disease	1 (6%)	10 (11%)	n.s. <sup>b</sup>
Lung disease	0 (0%)	5 (5%)	n.s. <sup>b</sup>
Liver disease	2 (12%)	6 (7%)	n.s. <sup>b</sup>
Renal disease	0 (0%)	4 (4%)	n.s. <sup>b</sup>
Lifestyle habit			
Drinking	10 (59%)	43 (47%)	n.s. <sup>b</sup>
Smoking	1 (6%)	12 (13%)	n.s. <sup>b</sup>

\*mean ± standard deviation

<sup>a</sup>: Mann-Whitney U test; <sup>b</sup>: Fisher's exact test; n.s.: not significant

Table 2. Intraoperative and postoperative factors of the patients

	Patients with postoperative delirium ( <i>n</i> = 17)	Patients without postoperative delirium ( <i>n</i> = 92)	<i>P</i> -value
Surgery type			n.s. <sup>b</sup>
Laparotomy	9 (53%)	31 (34%)	
Laparoscopy	8 (47%)	61 (66%)	
Operation time (minutes)*	270.4 ± 114.4	241.9 ± 89.8	n.s. <sup>a</sup>
Anesthesia time (minutes)*	325.9 ± 117.6	300.8 ± 93.8	n.s. <sup>a</sup>
Blood loss (ml)*	217.1 ± 351.1	144.8 ± 236.5	n.s. <sup>a</sup>
Blood transfusion	3 (18%)	10 (11%)	n.s. <sup>b</sup>
Day after blood-test findings			
Albumin (g/dl)*	2.8 ± 0.4	2.9 ± 0.6	n.s. <sup>a</sup>
Calcium (mg/dl)*	7.9 ± 0.4	8.0 ± 0.4	n.s. <sup>a</sup>
C-reactive protein (mg/dl)*	7.3 ± 2.7	7.7 ± 3.6	n.s. <sup>a</sup>

\*mean ± standard deviation

<sup>a</sup>: Mann-Whitney U test ; <sup>b</sup>: Fisher's exact test ; n.s. : not significant

### Multivariate analysis

Logistic regression analysis indicated that only Helplessness/Hopelessness score (MAC scale) was a significant risk factor for postoperative delirium (odds ratio, 1.356 ; 95% confidence interval, 1.082-1.698 ; *P* < 0.01) (Table 4).

## DISCUSSION

The incidence of postoperative delirium is strongly influenced by the patient's profile and the type of surgery. The incidence of postoperative delirium has varied greatly in previous reports : 9% after non-cardiac surgery in patients 50 years or older<sup>20</sup> ; 17% after hepatectomy<sup>6</sup> ; 41.7% after cardiac surgery<sup>21</sup> ; and 54.7% after vascular, orthopedic, or gastrointestinal surgery in patients 75 years or older<sup>2</sup>. In a study that included patients with profiles and types of surgery similar to those of our patients, the incidence of postoperative delirium in patients who were 70 years or older and had gastric or colorectal cancer was 19.0%<sup>22</sup>, which was similar to the rate of 15.6% in the present study. Therefore, the incidence of postoperative delirium did not differ greatly between the preceding study and the present study.

We found that the Helplessness/Hopelessness subscale score of the MAC scale was significantly higher in patients who had postoperative delirium than in those who did not. Of all the categories of psychological adjustment to cancer, helplessness and hopelessness are considered harmful psychological responses<sup>23</sup>. In contrast, fighting

spirit is considered a beneficial psychological response<sup>24</sup>. The Helplessness/Hopelessness score is inversely correlated with the Fighting Spirit score<sup>16</sup>. In the present study, univariate analysis showed that the Fighting Spirit score was significantly lower in patients with postoperative delirium (although logistic regression analysis failed to show such a significant difference) and showed an opposite trend for the Helplessness/Hopelessness score.

In the present study several items showed substantial variability among patients. For example, the Helplessness/Hopelessness score ranged from 6 to 22 points, and the Fighting Spirit score ranged from 32 to 64 points. A major premise of our study was that the subjects had been told, before they were admitted to the hospital or had surgery they had elected to undergo, that gastric or colorectal cancer had been diagnosed. What must be considered separately from their consent to surgery, however, is that patients differ greatly in how they respond psychologically to being told they have a severe illness, such as cancer, and how they deal with it. For example, when they are first told they have cancer, patients tend to be extremely shocked, to deny they have cancer, and to feel despair. They then have periods of anxiety, anguish, and depression. Two to 3 weeks after being told they have cancer, most patients have accepted the truth of their condition and are attempting to adjust positively<sup>25</sup>. However, patients are also likely to have lingering anxiety or depression when they are admitted to the hospital and undergo surgery.

Although few studies have examined the association

Table 3. The results of psychological tests

	Patients with postoperative delirium (n = 17) (mean ± SD)	Patients without postoperative delirium (n = 92) (mean ± SD)	P-value*
HADS			
Anxiety score	7.7 ± 3.6	5.5 ± 3.5	< 0.05
Depression score	6.5 ± 4.6	4.3 ± 3.6	n.s.
GHQ-28			
Total score	10.0 ± 5.5	6.2 ± 5.1	< 0.01
EORTC QLQ-C30			
Global health status			
Global	48.5 ± 15.9	51.3 ± 21.5	n.s.
Functional scales			
Physical	78.4 ± 19.9	84.1 ± 15.9	n.s.
Role	73.5 ± 27.0	85.6 ± 21.6	< 0.05
Emotional	72.1 ± 14.7	76.3 ± 17.1	n.s.
Cognitive	68.6 ± 21.1	73.2 ± 22.2	n.s.
Social	75.5 ± 19.6	77.4 ± 19.5	n.s.
Symptom scales			
Fatigue	30.0 ± 16.1	28.0 ± 21.1	n.s.
Nausea and vomiting	2.9 ± 8.8	1.6 ± 6.6	n.s.
Pain	12.7 ± 19.1	13.0 ± 19.1	n.s.
Dyspnoea	9.8 ± 15.6	14.1 ± 22.2	n.s.
Insomnia	21.6 ± 35.2	19.6 ± 26.2	n.s.
Appetite loss	23.5 ± 25.7	12.0 ± 19.5	< 0.05
Constipation	47.0 ± 77.0	28.6 ± 30.3	n.s.
Diarrhoea	17.6 ± 26.7	18.1 ± 25.9	n.s.
Financial difficulties	29.4 ± 23.2	22.8 ± 23.7	n.s.
MAC scale			
Fighting Spirit	45.6 ± 6.3	50.0 ± 7.1	< 0.05
Helplessness/Hopelessness	13.8 ± 3.5	10.0 ± 3.3	< 0.001
Anxious Preoccupation	24.0 ± 3.6	23.2 ± 3.6	n.s.
Fatalism	22.9 ± 4.3	22.4 ± 3.6	n.s.
Avoidance	2.6 ± 1.1	2.4 ± 1.1	n.s.

HADS : Hospital Anxiety and Depression Scale ; GHQ-28 : 28-item version of the General Health Questionnaire ; EORTC QLQ-C30 : European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 ; MAC scale : Mental Adjustment to Cancer scale

SD : standard deviation

\*Mann-Whitney U test ; n.s. : not significant

between postoperative delirium and the psychological state of patients, some studies have found postoperative delirium to have a high incidence among patients with high levels of anxiety and depression<sup>8,9</sup>. In the present study, however, we observed no differences in anxiety and depression scores between patients who had postoperative delirium and those who did not, although preoperative anxiety was slightly, but not significantly, stronger in patients who had postoperative delirium.

Several previous studies have also identified the Help-

lessness/Hopelessness score as being closely associated with psychological conditions, such as depression and anxiety<sup>16,26</sup>. One study has found that an educational, cognitive therapy, which promotes coping strategies for anxiety and encourages patients with cancer to obtain information about their disease, reduces Helplessness/Hopelessness scores<sup>27</sup>. However, methods of reducing feelings of helplessness and hopelessness have not been adequately investigated. These reported trends suggest that alleviating patient anxiety and depression would indirectly reduce responses of helplessness.

Table 4. The results of logistic regression analysis

Variable	Odds ratio	95% confidence interval	P-value
HADS			
Anxiety score	1.033	0.856 - 1.248	n.s.
GHQ-28			
Total score	0.918	0.773 - 1.091	n.s.
EORTC QLQ-C30			
Role	0.983	0.960 - 1.008	n.s.
Appetite loss	1.007	0.977 - 1.038	n.s.
MAC scale			
Fighting Spirit	0.958	0.861 - 1.066	n.s.
Helplessness/Hopelessness	1.356	1.082 - 1.698	< 0.01

HADS : Hospital Anxiety and Depression Scale ; GHQ-28 : 28-item version of the General Health Questionnaire ; EORTC QLQ-C30 : European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 ; MAC scale : Mental Adjustment to Cancer scale  
n.s. : not significant

ness/hopelessness and, therefore, would reduce the incidence of postoperative delirium.

Because the patients of the present study had their psychological state directly assessed before surgery, they were not able to receive specific treatments or support for strong feelings of despair or anxiety. Therefore, a topic for future discussion is the development of a system in which the psychological state of patients can be monitored after they are informed of cancer so that those with strong feelings of despair, anxiety, or depression can be treated by psychiatrists and clinical psychologists.

The present study had several limitations. First, the study involved a single institution. A second limitation was that the subjects were patients who had previously been informed of primary gastric or colorectal cancers. A third limitation was that patients were excluded if a history of organic brain disease was revealed with an examination of the medical record or an interview. A fourth and final limitation of the present study was that observations were limited to the perioperative period. Because of these limitations, future studies should include a greater number of patients from multiple institutions, data from patients with recurrent cancers or cancers of other organs, and long-term observations not restricted to the perioperative period.

### CONCLUSION

Our study has found that among patients with gastric or colorectal cancer, Helplessness/Hopelessness score is

significantly higher in patients with postoperative delirium. Our findings show that patients who have strong helplessness and hopelessness before surgery are at a high risk for postoperative delirium.

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