





**ORIGINAL ARTICLE**

# Grip strength as a predictor of postoperative delirium in patients with colorectal cancers

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**Abstract**

**Background:** The population is aging rapidly, and the population of patients who undergo surgeries is aging, too. Elderly patients have much risk of postoperative delirium, which increases the number of adverse events. The aim of this study was to investigate the risk factors of postoperative delirium in elderly patients with colorectal cancer.

**Methods:** We conducted a retrospective cohort analysis of consecutive patients aged 70 years and older who underwent surgeries for colorectal cancer at our department in the period from May 2012 to October 2019. We investigated the correlation between the incidence of postoperative delirium and Comprehensive Geriatric Assessment (CGA) scores, comorbidities, and perioperative factors. Postoperative delirium was retrospectively diagnosed by checking clinical records.

**Results:** Postoperative delirium was diagnosed in 36 of 271 patients (13.3%) with colorectal cancer. Among many comorbidities, only renal disease was significantly associated with postoperative delirium. Among the items in the CGA, age; Mini-Mental State Exam (MMSE), Barthel Index, Instrumental Activities of Daily Living (IADL), Vitality Index, and Geriatric Depression Scale (GDS) scores; and grip strength were associated with postoperative delirium. Among perioperative factors, blood transfusion was associated with postoperative delirium. Multivariate logistic regression analysis identified older age, MMSE, GDS, and grip strength as significant independent risk factors for postoperative delirium.

**Conclusions:** This single-center retrospective observational study demonstrated that grip strength is an independent predictor of postoperative delirium, along with age, MMSE, and GDS.

**KEYWORDS**

colorectal cancer, grip strength, postoperative delirium

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## 1 | INTRODUCTION

Of all cancers, colorectal cancer (CRC) has the third highest incidence and is the second leading cause of cancer death worldwide, according GLOBOCAN 2018 data.<sup>1</sup> CRC is 3–4 times more common in developed than in developing nations, and its incidence is rising steadily in developing nations.<sup>1</sup>

The population is aging rapidly worldwide, and patients with cancer are aging, too. Because chemotherapy has been improved and surgical techniques have also been improved and become less invasive, the population of patients who undergo operation for colorectal cancers is aging. Elderly patients with cancers tend to have more postoperative complications and more adverse events with chemotherapy than middle-aged patients.

Frailty is a common focus of study in recent years because we must take measures to treat elderly patients before they experience postoperative complications and adverse events of chemotherapy. Frail patients are vulnerable to stressors and have reduced ability to maintain or regain homeostasis after a destabilizing event.<sup>2</sup> Frailty increases the risk of adverse events including falls, delirium, and disability.<sup>3</sup> In particular, the incidence of not only delirium but also postoperative delirium is high in elderly patients for both emergency and elective surgery,<sup>4</sup> and Olin has reported that approximately half of elderly patients in his study developed this condition.<sup>5</sup>

Perioperative patients are exposed to many factors that may lead to delirium, particularly pain and environmental changes,<sup>6</sup> but there are also many predisposing factors that can cause delirium, such as dementia, depression, and dehydration.<sup>6</sup> Delirium has been associated with increased days of requiring mechanical ventilation, length of ICU, and hospital stay,<sup>7</sup> and is also associated with functional decline at 1 month after cardiac surgery. Delirium in older patients after elective surgery is reported to significantly increase adverse outcomes, including prolonged length of hospital stay, institutional discharge, and 30-day readmission,<sup>8</sup> and to worsen the survival curve in patients with advanced cancer.<sup>9</sup> Thus, we must predict postoperative delirium before operations and take measures to

avoid postoperative delirium beforehand. However, there are few clear and reliable predictors of postoperative delirium. The aim of this study was to identify the risk factors for postoperative delirium in elderly patients with colorectal cancers, based on preoperative evaluation using tests for frailty, including grip strength.

## 2 | PATIENTS AND METHODS

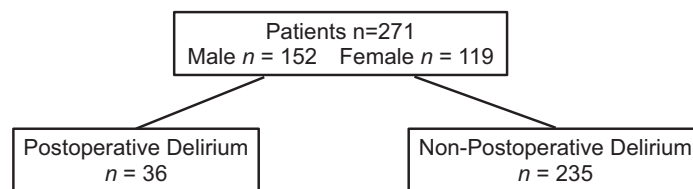
### 2.1 | Patients and preoperative factors

This retrospective study was approved by our institutional review board (approval No. 15144). All 271 patients aged  $\geq 70$  years who underwent surgery for colorectal cancers at Osaka University Hospital (Osaka, Japan) in the period from May 2012 through October 2019 were included in this study. There were 152 men and 119 women (Figure 1). We tested 10 kinds of diseases as potential risk factors for postoperative delirium. We checked whether patients had or did not have hypertension, diabetes mellitus, hyperlipidemia, thyroid disease, liver disease, renal disease, respiratory disease, brain disease, coronary artery disease, and psychiatric disease as a comorbidity, as one of the components of the Comprehensive Geriatric Assessment (CGA) (Figure 1).

We calculated the average of the right- and left-hand grip strengths, which we measured three times by use of a Smedley-type digital hand dynamometer (TK5401, Takei Scientific Instruments Co., Niigata Japan) before the surgery (Figure 1).

### 2.2 | Comprehensive geriatric assessment

We evaluated the patients on the basis of the CGA. The geriatricians in our institution evaluated the patients on the basis of the CGA at outpatient care unit before surgeries. The CGA is defined as a multidisciplinary diagnostic and treatment process that identifies medical, psychosocial, and functional limitations of a frail older person in



#### Preoperative Factors

- CGA (MMSE, Barthel Index, IADL, Vitality Index, GDS, Grip Strength)
- Comorbidities

(Hypertension, Diabetes mellitus, Hyperlipidemia, Thyroid / Liver / Renal / Respiratory / Brain / Coronary Artery / Psychiatric Disease )

#### Perioperative Factors

- Surgical approach
- Operation time
- Blood loss volume
- Blood transfusion
- Epidural anesthesia

MMSE : Mini-Mental Status Exam  
IADL : Instrumental Activities of Daily Living Scale  
GDS : Geriatric Depression Scale

FIGURE 1 Patient characteristics and preoperative and perioperative factors

order to develop a coordinated plan to maximize overall health with aging.<sup>10</sup> Core components of the CGA are functional capacity, cognitive impairment, depression, and comorbidity. We used the Mini-Mental Status Exam (MMSE), Barthel Index, Instrumental Activities of Daily Living (IADL), Vitality Index, and Geriatric Depression Scale (GDS) to evaluate each patient's status in terms of cognitive impairment, function in activities of daily living (ADL), vitality, and depression. We added grip strength to evaluate physical strength related to physical disability.

### 2.3 | Mini-Mental Status Exam (MMSE)

The Mini-Mental Status Exam (MMSE) is a widely used test of cognitive function among the elderly.<sup>11</sup>

### 2.4 | Barthel Index

The Barthel Index is an index of 10 skills related to basic activities of daily living such as feeding and going to the toilet.<sup>12</sup>

### 2.5 | The Lawton Instrumental Activities of Daily Living Scale (IADL)

The Lawton Instrumental Activities of Daily Living Scale (IADL) is an appropriate instrument to assess independent living skills, which are considered more complex than the basic activities of daily living.<sup>13</sup>

### 2.6 | Vitality Index

The Vitality Index is an index established to measure vitality related to activities of daily living and is composed of five subscales: walking pattern, communication, feeding, on and off toilet, and rehabilitation and other activities, with 10 scores in all.<sup>14</sup>

### 2.7 | The Geriatric Depression Scale (GDS)

The Geriatric Depression Scale (GDS) is a self-reported measure of depression in older adults.<sup>15</sup> In this study we used the shortened form of the GDS, comprising 15 items.

### 2.8 | Perioperative factors

This study considered elective resection as well as palliative surgeries, recurrent surgeries such as metastatic partial liver resection and metastatic lymphadenectomy, transanal endoscopic microsurgies, and colostomy surgeries. Elective resections were conducted in

254 patients, recurrence or metastasis surgeries in seven patients, transanal endoscopic microsurgies in seven patients, and colostomy surgeries in three patients. We assessed the perioperative factors, including surgical approach, operation time, blood loss volume, blood transfusion, epidural anesthesia, and hospital stay for risk of postoperative delirium.

### 2.9 | Diagnosis of postoperative delirium

We diagnosed delirium retrospectively by checking clinical records. In clinical records we looked for records of behavior of patients concerned with delirium. The records included the behavior of patients who slept during the day and were awake at night, hallucinated, removed infusion needles by themselves, behaved violently, and impaired orientation.

### 2.10 | Statistical analysis

Statistical analyses were performed using JMP Pro version 16 (SAS Institute, Inc, Cary, NC). Differences in age, sex, operative time, blood loss, blood transfusion, epidural anesthesia, Barthel Index, GDS, MMSE, Vitality Index, and grip strength were analyzed by use of Pearson  $\chi^2$  test. Statistical significance was established at  $P < .05$ . Variables that achieved significance at the 5% level on univariate analysis were entered into multivariate analysis to estimate the risk of postoperative delirium. Multivariate analysis was conducted using a multiple logistic regression model to adjust for multiple risk factors. We set the cutoff values of age (Figure S1), Barthel Index (Figure S2), GDS (Figure S3), MMSE (Figure S4), Vitality Index (Figure S5), IADL (Figure S6), grip strength (Figures S7, S8), and operation time (Figure S9) by using a ROC curve and divided the patients into two groups, a delirium group and a non-delirium group. We set the median blood loss volume as the cutoff value of blood loss volume.

## 3 | RESULTS

### 3.1 | Patients and preoperative factors

Data for 271 patients with colorectal cancer, including 152 men and 119 women, were analyzed. Table 1 presents the preoperative parameters: year, sex, and comorbidities. The median age of these patients was 80 years old (72-103 years old). Of all the 271 patients, 28 patients had cancer in cecum, 64 patients had cancer in ascending colon, 29 patients had cancer in transverse colon, 11 patients had cancer in descending colon, 59 patients had cancer in sigmoid colon, and 83 patients had cancer in rectum. Four patients had double colon cancers in the different areas. The comorbidities included hypertension, diabetes mellitus, hyperlipidemia, thyroid disease, liver disease, renal disease, respiratory disease, brain disease, coronary artery disease, and psychiatric disease.

**TABLE 1** Preoperative factors and comprehensive geriatric assessment

Patients and preoperative factors/CGA	n = 271
Age (years)	80 (72-103)
Sex (male/female)	152/119
Tumor location	
Cecum	28
Ascending colon	64
Transverse colon	29
Descending colon	11
Sigmoid colon	59
Rectum	83
Mini-mental state exam	26 (2-30)
Barthel index	100 (0-100)
Instrumental activities of daily living	8 (0-8)
Vitality index	10 (4-10)
Geriatric depression scale	2 (0-15)
Grip strength (kg)	
Male	27.1 (8-47.8)
Female	17.6 (2.8-47.8)
Hypertension -/+	151/120
Diabetes mellitus -/+	63/208
Hyperlipidemia -/+	102/169
Thyroid disease -/+	10/261
Liver disease -/+	5/266
Renal disease -/+	25/246
Respiratory disease -/+	21/250
Brain disease -/+	16/255
Coronary artery disease -/+	49/222
Psychiatric disease -/+	8/263

Abbreviation: CGA, Comprehensive Geriatric Assessment.

Table 2 presents the differences in comorbidities between the two groups in univariate analysis. Only renal disease differed significantly between the two groups ( $P = .0229$ ). There were no significant differences in the other diseases.

### 3.2 | Comprehensive geriatric assessment

Table 1 presents the items of comprehensive geriatric assessment. The median (range) scores on the MMSE, Barthel Index, IADL, Vitality Index, GDS, and median (range) grip strengths were, respectively, 26 points (2-30 points), 100 points (0-100 points), 8 points (0-8 points), 10 points (4-10 points), 2 points (0-15 points), and 27.1 kg for men (8-47.8 kg) and 17.6 kg for women (2.8-47.8 kg).

Table 3 shows the differences in the items of comprehensive geriatric assessment between the delirium and non-delirium groups in univariate analysis. Age was significantly different in the two groups ( $P = .0009$ ), but there were no significant sex differences between

the two groups ( $P = .1306$ ). All the preoperative factors used to evaluate the elderly—the MMSE, Barthel Index, IADL, Vitality Index, GDS, and grip strength—differed significantly between the two groups ( $P < .05$ ).

### 3.3 | Perioperative and postoperative factors

Table 4 shows the perioperative factors examined in this study. Laparoscopic surgeries were performed in 256 patients, and open surgeries in 15 patients. In four patients in the open surgery group the surgeries were switched from laparoscopic surgery to open surgery. The median (range) of the operation time and blood loss volume were 226 min (37-1001 min) and 30 mL (0-3700 mL). Of all 271 patients, 11 received a blood transfusion and only seven received epidural anesthesia. The median (range) hospitalization time was 20 days (9-94 days). Of all 271 patients, 254 patients were discharged and went back home, but 17 patients were transferred to another hospital because they could not go back home. Of 254 patients who were discharged and went back home, only nine patients were hospitalized again within 30 days after the surgeries.

The median (range) duration of postoperative delirium was 2 days (1-10 days). Of all 271 patients, 63 patients had postoperative complications. The complications included 21 bowel obstructions, 15 incisional surgical site infections (SSI), 13 Organ/Space SSIs, 10 urinary tract infections, seven cases of pneumonia, five cases of neurogenic bladder dysfunction, three cases postoperative bleeding, two cases of enteritis, two cases of deep vein thrombosis, one case of necrosis of stoma, one case of prostatitis, one case of cellulitis, one case of pancreatitis, one case of pulmonary edema, and one case of heart failure.

Table 5 shows the differences in perioperative and postoperative factors between the two groups. In the perioperative factors, only the blood transfusion differed significantly between the two groups ( $P = .0213$ ). There were no significant differences in the other perioperative factors. In the postoperative factors, the length of hospital stay and the readmission within 30 days after surgeries were not significantly different in the two groups, but the institutional discharge was increased in the delirium group than in the non-delirium group ( $P = .0430$ ). The incidence of postoperative complications was higher in the delirium group than in the non-delirium group ( $P = .0170$ ).

### 3.4 | Multivariate analysis

Multiple logistic regression analysis using age, MMSE, Barthel Index, IADL, Vitality Index, GDS, grip strength, renal disease, blood transfusion, and postoperative complications identified age, MMSE, and grip strength as significant independent determinants of postoperative delirium. ( $P = .0053$ ,  $P = .0001$ , and  $P = .0376$ , respectively) (Table 6). This result suggests that postoperative delirium is associated with age, MMSE, and grip strength in elderly patients with colorectal cancer.

**TABLE 2** Comparison of preoperative factors between the groups of patients with or without postoperative delirium

Preoperative factors (Comorbidities)	Postoperative delirium (+) n = 36	Postoperative delirium (-) n = 235	P value
Hypertension (+/-)	22/14	129/106	NS
Diabetes mellitus (+/-)	9/27	54/181	NS
Hyperlipidemia (+/-)	14/22	88/147	NS
Thyroid disease (+/-)	1/35	9/226	NS
Liver disease (+/-)	1/35	4/231	NS
Renal disease (+/-)	7/29	18/217	<.05
Respiratory disease (+/-)	3/33	18/217	NS
Brain disease (+/-)	3/33	13/222	NS
Coronary artery disease (+/-)	6/30	43/192	NS
Psychiatric disease (+/-)	3/33	5/230	NS

**TABLE 3** Comparison of Comprehensive Geriatric Assessment scores between the groups of patients with or without postoperative delirium

Comprehensive geriatric assessment	Postoperative delirium (+) n = 36	Postoperative delirium (-) n = 235	P value
Age ( $\geq 78$ / $< 78$ )	32/4	142/93	<.01
Sex (male/female)	18/20	136/99	NS
MMSE ( $\geq 23$ / $< 23$ )	17/19	205/30	<.0001
Barthel Index ( $\geq 95$ / $< 95$ )	24/12	214/21	<.0001
IADL ( $> 6.0$ / $\leq 6.0$ )	18/18	169/66	<.01
Vitality Index ( $\geq 9$ / $< 9$ )	30/6	224/11	<.01
GDS ( $\geq 4$ / $< 4$ )	21/15	74/161	<.01
Grip strength (kg)	13/21	180/48	<.0001
Male ( $\geq 21.8$ / $< 21.8$ )			
Female ( $\geq 15.4$ / $< 15.4$ )			

Abbreviations: GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living scale; MMSE, Mini-Mental State Exam.

## 4 | DISCUSSION

Postoperative delirium is defined as an acute change in cognitive status characterized by fluctuating consciousness and inattention occurring within 30 days after an operation.<sup>16</sup> The incidence of postoperative delirium is reported to vary widely, ranging from about 8% to more than 70% in various fields,<sup>17,18</sup> and the incidence varies with the kind of surgery. Although the incidence of postoperative delirium in patients with colorectal cancer is reported to be 10%-20%,<sup>16,19</sup> which is not very frequent, the aging population is increasing at an unprecedented rate, and the number of operations performed on elderly patients is increasing. Moreover, due to improvements in operative and anesthetic care and the development of less invasive operative techniques, more patients are considered for major colorectal operation. Elderly patients have a much higher risk of postoperative delirium, so the population of patients with postoperative delirium will be increasing.

Postoperative delirium after elective surgery is reported to increase adverse outcomes, including prolonged length of hospital stay, institutional discharge, and 30-day readmission.<sup>8</sup> It has been

reported that mortality and discharge to a nursing home are also significantly higher.<sup>20</sup> Thus, postoperative delirium may have a bad influence on not only the patients but also their families. If the occurrence of delirium could be predicted before surgery, it might be a decisive factor for the patients and family members in considering surgery. Therefore, we examined the factors that might correlate with postoperative delirium and that can be easily obtained preoperatively.

In past reports, the incidence of postoperative delirium in patients with colorectal cancer has been 10%-20%.<sup>16,19</sup> In this study, the incidence of postoperative delirium was 13.8%, which is comparable. Univariate analyses have shown that a history of psychiatric disease is associated with postoperative delirium after major abdominal surgeries ( $P = .003$ ).<sup>21</sup> A history of psychiatric disorder has been associated with postoperative delirium in elderly patients with esophagectomy ( $P = .017$ ).<sup>22</sup> Diabetes mellitus has been associated with postoperative delirium after thoracic surgery ( $P = .04$ ).<sup>23</sup> In our study, the incidence of postoperative delirium was significantly different in patients with none of these diseases. It is possible that because our study included fewer patients with psychiatric disease or diabetes mellitus than the

other studies, psychiatric disease and diabetes mellitus did not differ significantly between our delirium and non-delirium groups.

The laparoscopic approach has been associated with postoperative delirium.<sup>21</sup> However, in this study the incidence of postoperative delirium did not differ significantly between the laparoscopic surgery group and the open surgery group ( $P = \text{NS}$ ). This suggests that, because almost all the patients (256 of 271; 94.5%) were treated laparoscopically, the open approach was not a risk factor for postoperative delirium in our study. Among intraoperative characteristics, only blood transfusion was associated with the incidence of postoperative delirium; blood loss volume was not. In some reports, blood loss and operative time have been associated with postoperative delirium.<sup>16,19</sup> High blood loss ( $\geq 400$  mL) has been reported as a risk factor for postoperative delirium,<sup>19</sup> as has receipt of blood transfusions.<sup>24</sup>

TABLE 4 Perioperative and postoperative factors

Perioperative factors	n = 271
Laparoscopic/open surgery	256/15
Operation time (min)	226 (37-1001)
Blood loss volume (mL)	30 (0-3700)
Blood transfusion +/-	11/260
Epidural anesthesia +/-	7/264
Hospital stay (days)	20 (9-94)
Institutional discharge +/-	17/254
30-day readmission +/-	9/245
Postoperative complications +/-	63/208 (23.2%)
Bowel obstruction	21 (7.7%)
Incisional SSI	15 (5.5%)
Organ/Space SSI	13 (4.8%)
Urinary tract infection	10 (3.7%)
Pneumonia	7 (2.6%)
Neurogenic bladder dysfunction	5 (1.8%)
Postoperative bleeding	3 (1.1%)
Others	10 (3.7%)

Abbreviation: SSI, surgical site infection

Consistent with the former, this study suggested that high blood loss ( $\geq 520$  mL) is associated with the incidence of postoperative delirium ( $P < .05$ ). Almost all the operations in this study were laparoscopic, and blood loss in almost 80% of all cases was less than 200 mL. If we had set the cut-off value of blood loss as 520 mL, this study would have become very biased, so we set the cut-off value of blood loss as the median volume, 30 mL. Furthermore, almost all the patients who received blood transfusion and had postoperative delirium had high blood loss ( $\geq 520$  mL), so blood transfusion was associated with the incidence of postoperative delirium ( $P < .05$ ).

In some reports, delirium in older patients is reported to significantly increase adverse outcomes, including prolonged length of hospital stay, institutional discharge, and 30-day readmission.<sup>8</sup> In this study, the length of hospital stay and the 30-day readmission were not significantly different between the two groups, but the institutional discharge was increased in the delirium group than in the non-delirium group ( $P = .0430$ ). In our study the incidence of postoperative complications was higher in the delirium group than in the non-delirium group. Tei et al reported that there were significant differences in terms of Organ/Space SSI, cardiac or pulmonary disease between the delirium group and the non-delirium group.<sup>16</sup> We divided the postoperative complications into small categories: bowel obstruction, incisional SSI, Organ/Space SSI, pneumonia, and urinary disorders. There were not significant differences in terms of bowel obstruction, incisional SSI, Organ/Space SSI, pneumonia, and urinary disorders between the two groups.

Barthel Index, Vitality Index, MMSE, IADL, and GDS scores have been found to be associated with the incidence of postoperative delirium in patients with gastrointestinal cancer.<sup>25</sup> MMSE and GDS scores have been associated with postoperative delirium in patients with esophageal cancer,<sup>22</sup> and GDS score has been found to be an independent predictor of postoperative delirium.<sup>26</sup> In our study, the MMSE, Barthel Index, Vitality Index, and GDS scores were associated with the incidence of postoperative delirium, and MMSE was an independent risk factor for postoperative delirium. The Barthel Index, Vitality Index, and GDS scores were not independent risk factors for postoperative delirium, but grip strength was. In cardiac surgery

TABLE 5 Comparison of perioperative and postoperative factors between the groups of patients with or without postoperative delirium

Perioperative Factors	Postoperative delirium (+) n = 36	Postoperative delirium (-) n = 235	P value
Laparoscopic/open surgery	33/3	223/12	NS
Operation time ( $\geq 200$ / $< 200$ )	26/10	142/93	NS
Blood loss volume ( $\geq 30$ / $< 30$ )	23/13	131/104	NS
Blood transfusion +/-	4/32	7/228	$< .05$
Epidural anesthesia +/-	2/34	5/230	NS
Postoperative complications +/-	14/22	186/49	$< .05$
Hospital stay ( $\geq 20$ / $< 20$ )	18/18	118/117	NS
Institutional discharge +/-	5/31	12/223	$< .05$
30-day readmission +/-	1/30	8/215	NS

Abbreviation: SSI, surgical site infection.

**TABLE 6** Multivariate analysis of preoperative and perioperative factors

Preoperative/perioperative factors	Multivariate OR (95% CI)	P value
Age ( $\geq 78$ )	4.66 (1.37-15.86)	<.05
MMSE (<23)	5.64 (2.29-13.90)	<.01
Barthel Index (<95)	1.72 (0.54-5.52)	NS
Vitality Index (<9)	1.57 (0.37-6.74)	NS
IADL ( $\leq 6$ )	1.23 (0.47-3.21)	NS
GDS ( $\geq 4$ )	2.22 (0.93-5.33)	NS
Renal disease (+)	2.89 (0.87-9.64)	NS
Blood transfusion (+)	1.36 (0.26-7.14)	NS
Postoperative complications (+)	1.82 (0.72-4.61)	NS
Grip strength (kg) (<21.8/15.4)	2.78 (1.07-7.22)	<.05

Abbreviations: GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living scale; MMSE, Mini-Mental State Exam.

patients, grip strength has been associated with the incidence of postoperative delirium ( $P = .0347$ ),<sup>27</sup> but there are few reports in which grip strength in patients with colorectal cancer has been associated with postoperative delirium. This study is probably the only one in which grip strength has been identified as one of the independent risk factors for postoperative delirium in patients with colorectal cancer.

In some reports, grip strength has been associated with cognitive function in aging people. Grip strength across time is associated with the decline of verbal ability, spatial ability, processing speed, and memory after age 65, and study participants with greater grip strength are expected to have less cognitive decline.<sup>28</sup> This suggests that baseline global cognitive function and change in global cognitive function are associated with declines in physical performance. Decline in the Modified Mini-Minimal State Examination score has been found to be significantly associated with decline in grip strength. A weak handgrip is associated not only with lower MMSE scores but also lower Digit Symbol Substitution Test scores, which are measures of general and unspecific processing speed and are more sensitive to slight changes in higher-level cognition than the MMSE. When comparing participants with the weakest grip strength, those with the strongest handgrip strength showed less severe cognitive decline as measured by the MMSE and DSST.<sup>29</sup> Hatabe et al reported that lower handgrip strength in late life is significantly associated with the development of total dementia, including Alzheimer's disease and vascular dementia.<sup>30</sup> They listed several possible explanations for this relationship. First, higher handgrip strength may be a proxy for the presence of habitual exercise. Habitual exercise promotes the maintenance of greater muscle strength and improvement of cardiovascular function, health benefits that improve cognitive function. Second, lower handgrip strength is an indicator of frailty, which is characterized by multisystem impairments including reduced systemic muscle strength. Frailty increases the risk of adverse events, including delirium.<sup>3</sup> Third, lower handgrip strength may reflect systemic inflammation, which has been linked to cognitive decline.<sup>30</sup> On the other hand, MMSE has been associated with postoperative delirium in some reports,<sup>22,25</sup> so it is possible that grip strength

is related to postoperative delirium. Thus, our finding that grip strength is an independent risk factor for postoperative delirium is reasonable.

This study has several limitations. Since it is retrospective and delirium was diagnosed by checking clinical records, the diagnosis of postoperative delirium might be biased. We should diagnose delirium at the onset of delirium by clear delirium standards such as Confusion Assessment Method (CAM) and *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)*. We should also diagnose delirium by some nurses or doctors because the diagnosis of delirium might be biased if only one staff diagnosed delirium. We will diagnose delirium of patients with colorectal cancer at the onset of delirium and identify any other risk factors of postoperative delirium prospectively. Furthermore, because the study included many kinds of surgeries, including palliative surgeries, and patients from Stage 0 to Stage IV, the incidence of postoperative delirium might be biased. Postoperative complications such as surgical site infection, anastomotic leakage, hemorrhage, and ileus were not analyzed, although Tei et al found that organ/space surgical site infection is associated with the incidence of postoperative delirium.<sup>16</sup> Our purpose was to identify the preoperative risk factors for postoperative delirium, but we must also analyze postoperative complications with preoperative factors.

In this study, we used the cutoff values which were different from those used in general.

The cutoff values of MMSE and GDS, which are used generally, are 24 points and 5 points. In this study, we set the cutoff values of MMSE and GDS as 23 points and 4 points by ROC curves. The cutoff values of grip strength used generally are 28 kg for men and 18 kg for women, but in this study, we set the cutoff values of grip strength as 21.8 kg for men and 15.4 kg for women by ROC curves. All the patients of this study have cancers of Stage I-IV, and the general conditions of them may be worse than healthy elderly patients, so the cutoff values which we used in this study were lower than those used in general.

In conclusion, grip strength is an independent predictor of postoperative delirium, along with the MMSE, GDS, and age  $\geq 78$ . Grip strength is easier to measure than CGA scores such as those of the MMSE, Barthel Index, Vitality Index, and GDS, so grip strength should be used as a predictor of postoperative delirium, for which we should prepare for before surgeries.

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#### DISCLOSURE

Conflicts of interest: The authors declare that they have no conflicts of interest regarding this study.

The Human Ethics Review Committee of Osaka University Graduate School of Medicine approved the protocol for this case report and this report conforms to the provisions of the Declaration of Helsinki in 1995. The subject provided informed consent, and patient anonymity was preserved. We declare no conflict of interests for this article. The items of the registry of the study and animal studies are not applicable.

Ethical approval: The Human Ethics Review Committee of Osaka University Graduate School of Medicine approved the protocol for this case report, and this case report conforms to the provisions of the 1995 Declaration of Helsinki.

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