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**Original Article** 

# Does pre-operative physical rehabilitation improve the functional outcomes of patients undergoing gastrointestinal cancer surgery?

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Abstract. [Purpose] This study aimed to evaluate the effectiveness of pre-operative physical rehabilitation on the postoperative course of the patients with gastrointestinal cancer undergoing surgery. [Participants and Methods] A rehabilitation physician examined and educated 33 patients (42% of whom were male with a mean age of  $65.2 \pm$ 10.9 years) who were scheduled to undergo elective surgery for gastrointestinal cancer. They received instructions for performing exercise from a physical therapist 17.0 ± 7.3 days prior to surgery. We divided the participants into three groups (improvement, maintenance, and deterioration) based on the changes in their ability to walk prior to surgery. This study compared the results of the 6-min walk test, hospital anxiety and depression scale, and 36-Item Short-Form Health Survey version 2 for the three groups at baseline, following rehabilitation prior to surgery, and 4 weeks following surgery. [Results] In the improvement group, the decrease in the ability to walk between the baseline and 4 weeks after surgery was not significant. Conversely, the deterioration group exhibited a significant decrease in the ability to walk 4 weeks after surgery. [Conclusion] Improvement in walking ability by rehabilitation training prior to surgery leads to the preservation of physical function in the patients with gastrointestinal cancer undergoing surgery.

Key words: Gastrointestinal cancer surgery, Physical function, Pre-operative physical rehabilitation

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### **INTRODUCTION**

Pre-operative physical conditioning by such as inspiratory muscle training or exercise training is a common strategy influencing the postoperative outcomes of patients, including length of stay, exercise capacity, cognitive function, and perioperative complications<sup>1-4</sup>). In the field of cancer rehabilitation, preventive rehabilitation prior to surgery may reduce postoperative complications and mortality<sup>5</sup>). Recently, an increase in the number of reports of reducing hospital length stay or postoperative complications and increasing physical function or quality of life by preventive rehabilitation such as moderate level aerobic exercise training and resistance exercise training prior to surgery has been observed in patients with gastrointestinal cancer (e.g., reports comparing postoperative outcomes and verifying intervention effect)<sup>6, 7</sup>). However, information on preventive pre-operative rehabilitation for cancer patients in Japan is scarce.

In this study, a hypothesis formulated that an increase in exercise capacity by rehabilitation training prior to surgery for patients with gastrointestinal cancer may reduce the postoperative adverse events, such as frequency of postoperative

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complications, declining physical function, and quality of life. This study aimed to determine how pre-operative changes in physical function due to rehabilitation training can influence the frequency of postoperative complications, postoperative physical function, health-related quality of life (HRQOL), and mental status in surgical patients with gastrointestinal cancer.

### **PARTICIPANTS AND METHODS**

The present study is a prospective observational single-site study. It was conducted at the International University of Health and Welfare, Mita Hospital, which was accredited as a Tokyo-designated cancer treatment hospital between March 1, 2016, and December 31, 2017. The study was approved by the Research Ethics Board of the International University of Health and Welfare, Mita Hospital, Minato-ku, Tokyo, Japan, and study procedures were performed in accordance with the ethical standards (registration: 5-16-2). Moreover, the research was conducted based on the Declaration of Helsinki.

The participants of present study included all the patients who underwent elective surgical treatment for suspected or confirmed gastrointestinal cancer at the International University of Health and Welfare, Mita Hospital. The follow-up period of participant was 4 weeks after the surgical treatment from the time when elective surgery for gastrointestinal cancer was confirmed. The exclusion criteria were as follows: if surgery was performed as an emergency, if the patient's activities of daily living were limited, if the rehabilitation physician determined that pre-operative physical rehabilitation adversely affected the patient's medical condition (e.g., bone metastasis), if the patient received neoadjuvant therapy, if the patient could only exercise  $\leq 3$  days a week, or if home discharge was impractical.

All participants were examined and received patient education from the rehabilitation physician. To assess for diseases and the general condition of the patient that may affect pre-operative physical rehabilitation, medical examination was performed. In addition, the patients were instructed to take increased daily protein intake based on the guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN)<sup>8</sup>). Perioperative care for all paticipants was provided by a gastrointestinal surgeon based on the clinical pathway for surgery of gastrointestinal cancer of the International University of Health and Welfare, Mita Hospital. All patients were given direct exercise instruction by a physical therapist in a 1-h session. The exercise program prescription consisted of up to 50 min of unsupervised home-based exercise that alternated between aerobic and resistance exercise. The exercise program included a 5-min warm-up session, followed by 20 min of aerobic exercise and 20 min of resistance exercise, and culminated with a 5-min cool-down session. Aerobic exercises could include walking, jogging, swimming, or cycling at the patient's discretion. The exercise intensity in all participants was set in 50% of predicted maximum heart rate. Resistance exercises, such as squats, were also performed. The patients recorded their exercise status in a record book. Moreover, the intervention period was defined as the first session of direct exercise to the day prior to surgery; the number of intervention days was measured from the number of exercise days performed during the intervention period; and the exercise rate was expressed as percentage of the number of intervention days/intervention period.

The study parameters that were evaluated were exercise capacity, frequency of postoperative complications 1 month following surgery, mental status, and HRQOL.

Exercise capacity was evaluated using 6MWT based on the guideline of the American Thoracic Society<sup>9</sup>). The patients were instructed to walk back and forth a 50-m stretch of the hallway for 6 min at pace, which would require maximum effort by the end of the walk. The patients' exercise capacity was evaluated at three points: baseline (before rehabilitation), before surgery, and 4 weeks following surgery. In this study, the participants were divided into three groups based on the 6MWT results at the baseline assessment: the improvement group (an increase of  $\geq 14$  m), the maintenance group (an increase of  $\leq 14$  m), and the deterioration group (a decrease of  $\geq 14$  m)<sup>10</sup>. In this study, the total distance (in meters) covered in 6 min was recorded only once at each evaluation.

Based on the existing medical records, the frequency of postoperative complications was graded using the Clavien-Dindo classification<sup>11</sup>). Grade II or higher Clavien-Dindo classification was defined as the presence of postoperative complications<sup>12, 13</sup>).

The patients' mental status was evaluated using a Hospital Anxiety and Depression Scale (HADS)<sup>14</sup>). The HADS is a selfadministered questionnaire including two subscales of anxiety and depression; both subscales were evaluated in this study.

The HRQOL was evaluated using a 36-Item Short-Form Health Survey (SF36)<sup>15,16</sup>). SF36 is a self-administered questionnaire including eight subscales: physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health. In this study, the Japanese national standard values of eight subscales were calculated using a SF36 version 2 scoring program for the Japanese recommended by iHope International.

The following clinical data were prospectively collected from medical records: age at baseline, gender, clinical stage of cancer following surgery, comorbidities (hypertension, hyperlipidemia, diabetes mellitus, cardiac diseases, respiratory diseases, orthopedic diseases, and cerebrovascular diseases), diagnosis, type of surgery (laparoscopic or open surgery), surgery duration, blood loss, blood transfusion (red cell concentrates and fresh frozen plasma), baseline laboratory data (serum albumin and C-reactive protein), forced expiratory volume in 1 s (%) at baseline, and length of hospital stay.

The clinical characteristics (i.e., age, surgical time, blood loss, and laboratory data) of the three groups (improvement group, maintenance group, and deterioration group) were compared using the one-way analysis of variance (ANOVA) for continuous variables. Categorical variables (i.e., gender, clinical stage of cancer following surgery, comorbidities, and diagnosis) and the frequency of postoperative complications were compared using the  $\chi^2$  test.

The study parameters, such as 6MWT, HADS, and SF36, at baseline were compared among the three groups using the one-way ANOVA and Kruskal-Wallis test. Perioperative changes in parameters 4 weeks following surgery were compared using the two-way ANOVA of mixed-effects model. Subsequently, parameters with significant interaction effects were calculated as a change ratio of baseline and 4 weeks following surgery. The change ratios (change ratio=value after surgery/value before surgery \* 100%) of the three groups were compared using the one-way ANOVA and the Bonferroni multiple comparisons test. All statistical analyses were conducted using SPSS version 24.0 (SPSS Inc., Chicago, IL1, USA). A p-value <0.05 was considered statistically significant.

### **RESULTS**

A total of Two hundred and eighty eight (288) patients were identified as potentially eligible, of whom 33 patients were recruited; the rest, declined participation (172), did not meet the eligibility criteria (68) or had incomplete data (37). The participants were classified into the improvement group (26), maintenance group (12), and deterioration group (10) based on the capacity of variation of 6MWT at baseline. The baseline clinical characteristics of the three groups are presented in Table 1; no significant differences in the clinical characteristics between the groups were observed. The number of days of intervention, intervention period, and exercise rate during the pre-operative physical rehabilitation did not differ by group.

The baseline parameters of the three groups are presented in Table 2; no significant differences in the parameters studied by group were observed. The pre-operative physical rehabilitation study did not result in any significant adverse events, e.g., onset of new orthopedic diseases and cerebrovascular diseases.

Following surgery, 15 participants deviated from the normal course due to postoperative complications and could not be followed up, thus leaving 33 patients that were assessed at follow up. The majority of postoperative complications of gastrointestinal cancer were grades 0 to II (i.e., including deviation from the normal postoperative course, treatment with drugs, or blood transfusions for 26 patients) and grade III or IV (i.e., surgical and life-threatening complication for 7 patients). No significant differences between the groups based on the Clavien-Dindo classification grade (Table 1) were observed.

No significant difference among the three groups at baseline (Table 2) was observed. The 6MWT assessed 4 weeks following surgery significantly decreased when compared with that at baseline and before surgery (Table 3). Among the three groups, a significant interaction effect of 6MWT at baseline and the perioperative change on the 6MWT was found (Table 3). The calculated 6MWT change ratio indicated significant differences among the three groups; the 6MWT change ratio of the deterioration group was about 15% lower than that of the improvement group (Table 4). The pre-operative state of the patients in the improvement group was almost restored following surgery.

For the three groups, no significant differences between anxiety and depression scores at baseline (Table 2) or perioperatively (Table 3) were observed. For patients with gastrointestinal cancer, the median scores of anxiety and depression were lower than the cutoff points for adjustment disorder and major depressive disorder<sup>14</sup> at all-time points.

SF36 including eight subscales at baseline presented no significant differences among the groups. However, all groups exhibited poorer general health when compared with the Japanese national standard value of 50 (Table 2). The assessed physical function, physical role, bodily pain, vitality, and emotional role 4 weeks following surgery significantly decreased compared with those at baseline and prior to surgery. Moreover, the majority of subscales 4 weeks following surgery were lower than the Japanese national standard value of 50. Among the three groups, a significant interaction effect of 6MWT at baseline and the perioperative change on social functioning (Table 3) was found. The calculated social functioning change ratio did not differ among the groups (Table 4).

#### **DISCUSSION**

Mayo et al.'s studies that assessed physical exercise of colon cancer patients prior to surgery revealed that 29% of patients exhibited decreased exercise capacity<sup>17</sup>). In this study, pre-operative physical rehabilitation led to similar results to the Mayo studies, from the viewpoint of maintaining and improving exercise capacity<sup>17)</sup>. However, no significant differences in the clinical characteristics of each group of patients with gastrointestinal cancer were observed. Therefore, the cause of differences in the change in exercise capacity from pre-operative physical rehabilitation is unclear. In the future, pre-operative physical rehabilitation should be modified by physical function. Recently, Silver et al. advocated a comprehensive intervention referred to as "cancer prehabilitation", which begins between the diagnosis of cancer and the first treatment<sup>18, 19</sup>. The aim of cancer prehabilitation is to reduce physical dysfunction during and after treatment by assessing physical and mental function before treatment and providing comprehensive interventions, such as physical exercise, nutrition education, and mental health, to improve the baseline physical and mental function. In several previous studies on cancer prehabilitation for patients with gastrointestinal cancer, short-term effects, such as prevention of low physical function or low physical activity<sup>20-24</sup>), prevention of excessive reduction in body composition<sup>25</sup>), and prevention of low HRQOL, have been reported<sup>26</sup>). Furthermore, the long-term effects of prehabilitation in patients with gastrointestinal cancer included reduced mortality 1 year following surgery<sup>27</sup>). In the future, pre-operative physical rehabilitation should be modified to define the instruction for protein intake prior to surgery, management of each patient, and long-term intervention like that in previous studies of cancer prehabilitation<sup>22-25)</sup>. Also, pre-operative physical rehabilitation may be directed toward improving the exercise capacity of

Characteristics	Improvement group	Maintenance group	Deterioration group	
Mean age in years (SD)	62.6 (± 10.8)	71.6 (± 9.0)	62.3 (± 11.4)	
Gender				
Female	9 (56)	5 (50)	5 (71)	
Male	7 (44)	5 (50)	2 (29)	
Conser eliminal stars	, ()		= (=>)	
Cancer clinical stage	2 (10)	2 (20)	1 (14)	
0 I	3 (19) 2 (10)	2 (20)	1 (14)	
I H	5 (19) 4 (25)	3 (30) 1 (10)	4 (37)	
	4 (23) 5 (21)	1 (10)	2 (29)	
III N	5 (31)	2 (20)	0 (0)	
1v	1 (0)	0(0)	0 (0)	
Comorbidities*				
Hypertension	5 (31)	3 (30)	2 (29)	
Hyperlipidemia	3 (19)	0 (0)	0 (0)	
Diabetes mellitus	3 (19)	1 (10)	0 (0)	
Cardiac disease	3 (19)	0 (0)	0 (0)	
Respiratory disease	0 (0)	1 (10)	0 (0)	
Orthopedic disease	2 (13)	0 (0)	1 (14)	
Cerebrovascular disease	2 (13)	1 (10)	0 (0)	
None	9 (56)	6 (60)	3 (43)	
Diagnosis				
Esophageal cancer	3 (19)	0 (0)	0 (0)	
Gastric cancer	0 (0)	1 (10)	1 (14)	
Liver cancer	0 (0)	2 (20)	0 (0)	
Gallbladder cancer	0 (0)	0 (0)	1 (14)	
Bile duct cancer	3 (19)	0 (0)	0 (0)	
Pancreatic cancer	5 (31)	4 (40)	2 (29)	
Colon cancer	3 (19)	2 (20)	2 (29)	
Rectal cancer	2 (13)	1 (10)	1 (14)	
Type of surgery				
Open surgery	9 (56)	6 (60)	5 (71)	
Laparoscopic surgery	7 (44)	4 (40)	2 (29)	
Surgery duration (min)	306.4 (± 117.1)	242.2 (± 91.6)	279.3 (± 76.7)	
Blood loss (ml)	367.6 (± 513.6)	222.6 (± 258.2)	276.9 (± 299.2)	
Blood transfusion (mI)	( )		· · · · ·	
Red cell concentrates	$175.0(\pm 489.0)$	0.0(+0.0)	$80.0(\pm 211.7)$	
Fresh frozen plasma	$1/5.0 (\pm 290.2)$	$0.0 (\pm 0.0)$ 0.0 (+ 0.0)	$0.0 (\pm 0.0)$	
	105.0 (± 250.2)	0.0 (± 0.0)	0.0 (± 0.0)	
Laboratory data		0.2 (1.0.2)	0.2 (1.0.2)	
C-reactive protein (mg/dL)	$0.2 (\pm 0.3)$	$0.2 (\pm 0.2)$	$0.2 (\pm 0.3)$	
Serum albumin (g/dL)	$4.5 (\pm 0.2)$	$4.4 (\pm 0.4)$	$4.3 (\pm 0.3)$	
Baseline forced expiratory vol. at 1 s (%)	76.6 (± 7.5)	$77.1 (\pm 6.8)$	82.4 (± 4.7)	
Body mass index in kg/m <sup>2</sup>	22.2 (± 3.2)	23.5 (± 3.1)	20.7 (± 1.5)	
Dindo-Clavien classification				
Grade 0	4 (25)	8 (80)	4 (57)	
Grade I	5 (31)	2 (20)	1 (14)	
Grade II	5 (31)	2 (20)	3 (43)	
Grade III	3 (19)	0 (0)	0 (0)	
Grade IV	0 (0)	0 (0)	0 (0)	
Grade V	0 (0)	0 (0)	0 (0)	

 Table 1. Baseline clinical characteristics of patients with gastrointestinal cancer undergoing emergency surgery at the University of Health and Welfare, Mita Hospital, Japan, 2016–2017

#### Table 1. Continued

Characteristics	Improvement group (n=16)	Maintenance group (n=10)	Deterioration group (n=7)
Number of intervention days	15.9 (± 6.7)	14.9 (± 8.9)	14.3 (± 3.8)
Intervention period	17.7 (± 5.7)	17.4 (± 11.0)	14.7 (± 3.0)
Exercise rate	87.9 (± 19.4)	89.4 (± 17.0)	96.1 (± 10.3)
Length of hospital stay	24.3 (± 15.3)	15.4 (± 5.1)	18.1 (± 6.5)

Values are expressed as numbers (%) or mean  $\pm$  standard deviation.

Patients may have more than one comorbidity or may be in more than one Clavien-Dindo classification.

 Table 2. Baseline outcomes of patients with gastrointestinal cancer undergoing emergency surgery at the University of Health and Welfare, Mita Hospital, Japan, 2016–2017

Parameters	Improvement group	Improvement group Maintenance group	
	(n=16)	(n=16) (n=10)	
6MWT	537.0 (± 107.7)	564.1 (± 66.7)	562.2 (± 66.1)
HADS			
Anxiety	5.5 (0.0, 14.0)	5.0 (0.0, 11.0)	4.0 (3.0, 8.0)
Depression	3.5 (1.0, 10.0)	2.5 (0.0, 8.0)	3.0 (0.0, 10.0)
SF36 subscales			
Physical functioning	50.6 (10.9, 57.8)	52.4 (36.2, 57.8)	47.0 (39.8, 57.8)
Physical role	52.4 (29.1, 55.7)	45.8 (39.1, 55.7)	52.4 (35.8, 55.7)
Bodily pain	50.1 (35.8, 61.7)	61.7 (44.7, 61.7)	54.6 (35.8, 61.7)
General health	49.5 (27.1, 61.8)	49.5 (38.9, 69.8)	49.5 (35.1, 57.5)
Vitality	51.4 (37.0, 69.1)	56.3 (46.6, 69.1)	56.3 (30.6, 59.5)
Social function	53.8 (31.2, 57.0)	53.8 (24.8, 57.0)	50.6 (31.2, 57.0)
Emotional role	51.9 (18.6, 56.1)	51.9 (26.9, 56.1)	51.9 (47.7, 56.1)
Mental health	46.5 (30.4, 65.2)	58.5 (33.0, 65.2)	51.8 (35.7, 59.9)

Values are expressed as median (minimum value, maximum value) or mean ± standard deviation.

6MWT: 6-min walk test; HADS: Hospital Anxiety and Depression Scale; SF36: 36-Item Short-Form Health Survey.

patients with gastrointestinal cancer prior to surgery by focusing on the abovementioned content.

In this study, the 6MWT that was employed to determine the effect of pre-operative physical rehabilitation was a simple evaluation scale for cardiopulmonary reserve<sup>9, 28)</sup> capturing both increases in peripheral utilization of oxygen, such as by the skeletal muscle and entire interlocking lung–heart–vascular oxygen transport system<sup>29)</sup>, reflects oxygen intake, carbon dioxide excretion, and pulmonary blood flow<sup>28)</sup>. The postoperative complications are caused by multiorgan failure resulting from oxygen debt exceeding the oxygen requirements, which was accompanied by the immune response<sup>28, 30)</sup>. Patients with high cardiopulmonary reserve prior to surgery can adapt to the biological reaction associated with surgical stress following surgery because of their secure the oxygen requirements. However, the change in the exercise capacity of patients with gastrointestinal cancer prior to surgery did not significantly affect the rate of postoperative complication. The effect of the intervention provided to patients with gastrointestinal cancer in a previous study of cancer prehabilitation on the reduction of postoperative complications was not reported<sup>20–27)</sup>. In the future, it is important to examine in detail the impact of exercise capacity change on the onset of postoperative complications.

The effect of a change in exercise capacity through pre-operative physical rehabilitation exhibited a significant interaction effect on 6MWT and social functioning of SF36 subscale at baseline to 4 weeks following surgery. In the change ratio calculated at baseline and 4 weeks following surgery, 6MWT was only significantly higher in the improvement group as compared to that in the deterioration group. In the studies by Li et al., cancer prehabilitation for patients with gastrointestinal cancer has been shown to be effective in reducing the decline in HRQOL following surgery<sup>26</sup>. Pre-operative physical rehabilitation did not include interventions for the mental function of patients with gastrointestinal cancer in the perioperative period. The prevention of poor HRQOL of patients with gastrointestinal cancer following surgery may require comprehensive interventions requiring multiple specialties, such as clinical psychologist in the cancer prehabilitation studies by Li et al<sup>26</sup>. However, improved exercise capacity by pre-operative physical rehabilitation prior to surgery was significantly associated with a higher exercise capacity following surgery. Pre-operative physical rehabilitation corresponds to the single model that was

Parameters	Baseline (i)	Before surgery (ii)	4 weeks after surgery
Tarameters	Baseline (I) Belore surgery (II)		(iii)
6MWT *†			
Improvement group (n=16)	537.0 (± 27.2)	582.0 (± 27.2)	536.9 (± 27.2)
Maintenance group (n=10)	564.1 (± 20.2)	564.2 (± 20.2)	524.4 (± 20.2)
Deterioration group (n=7)	562.2 (± 27.2)	528.5 (± 27.2)	478.5 (± 27.2)
HADS – Anxiety			
Improvement group (n=16)	6.3 (± 0.9)	6.3 (± 0.9)	4.4 (± 0.9)
Maintenance group (n=10)	5.5 (± 1.0)	4.7 (± 1.0)	3.8 (± 1.0)
Deterioration group (n=7)	4.6 (± 0.8)	3.0 (± 0.8)	4.3 (± 0.8)
HADS – Depression			
Improvement group (n=16)	4.4 (± 0.7)	3.8 (± 0.7)	4.3 (± 0.7)
Maintenance group (n=10)	3.1 (± 1.0)	3.4 (± 1.0)	2.9 (± 1.0)
Deterioration group (n=7)	4.4 (± 1.5)	4.1 (± 1.5)	4.0 (± 1.5)
SF36 subscales – Physical functioning *			
Improvement group (n=16)	42.3 (± 3.3)	45.2 (± 3.3)	41.4 (± 3.3)
Maintenance group (n=10)	49.9 (± 3.5)	49.5 (± 3.5)	40.9 (± 3.5)
Deterioration group (n=7)	49.1 (± 3.9)	50.1 (± 3.9)	39.3 (± 3.9)
SF36 subscales – Physical role *			
Improvement group (n=16)	$47.9 (\pm 3.3)$	$44.5 (\pm 3.2)$	39.0 (± 3.3)
Maintenance group (n=10)	$47.1 (\pm 2.7)$	49.4 (± 2.6)	$45.3 (\pm 2.9)$
Deterioration group (n=7)	$49.6 (\pm 3.7)$	$48.7 (\pm 3.8)$	$36.2 (\pm 3.8)$
SF36 subscales - Bodily pain *			
Improvement group $(n=16)$	50.6 (+ 2.6)	50.7 (+ 2.6)	425(+27)
Maintenance group $(n=10)$	$57.4 (\pm 2.8)$	$55.5(\pm 2.8)$	$46.4 (\pm 2.8)$
Deterioration group $(n=7)$	$54.1 (\pm 2.0)$ 54.3 (+ 4.0)	$54.1 (\pm 4.0)$	$42.7 (\pm 4.0)$
SE2( subscales Consul Health	5 1.5 (± 1.0)	5 (= 1.0)	12.7 (= 1.0)
SF36 subscales – General Health	477(+10)	49.2 (+ 1.0)	49.5 (+ 1.0)
Improvement group (n=16)	$47.7 (\pm 1.9)$	$48.2 (\pm 1.9)$	$48.5 (\pm 1.9)$
Maintenance group $(n=10)$	$50.7 (\pm 3.1)$	$52.2 (\pm 3.1)$	$47.9 (\pm 3.1)$
SE2( subsceles Vitality *	47.3 (± 4.3)	49.2 (± 4.3)	48.8 (± 4.5)
SF36 subscales – vitality *	51.9 (1.2.2)	544(122)	40.9 (1.2.2)
Maintenance and the second second	$51.8 (\pm 2.3)$	$54.4 (\pm 2.3)$	$49.8 (\pm 2.3)$
Deterioration group (n=10)	$57.0 (\pm 5.4)$	$53.0 (\pm 3.4)$	$52.4 (\pm 5.4)$
Deterioration group (n-7)	32.2 (± 4.2)	34.9 (± 4.2)	47.1 (± 4.2)
SF36 subscales – Social function <sup>†</sup>			
Improvement group (n=16)	48.2 (±2.4)	50.6 (± 2.4)	39.4 (± 2.4)
Maintenance group (n=10)	47.4 (± 4.0)	46.1 (± 4.0)	49.6 (± 4.2)
Deterioration group (n=7)	46.0 (± 3.9)	49.7 (± 3.9)	43.2 (± 3.9)
SF36 subscales – Emotional role *			
Improvement group (n=16)	49.0 (± 2.7)	47.7 (± 2.7)	43.6 (± 2.7)
Maintenance group (n=10)	49.0 (± 3.4)	52.3 (± 3.4)	41.5 (± 3.4)
Deterioration group (n=7)	50.0 (± 4.4)	47.2 (± 4.4)	43.6 (± 4.4)
SF36 subscales – Mental health			
Improvement group (n=16)	45.6 (± 2.4)	49.6 (± 2.4)	49.1 (± 2.4)
Maintenance group (n=10)	54.2 (± 3.5)	51.6 (± 3.5)	50.2 (± 3.5)
Deterioration group (n=7)	51.4 (± 3.7)	54.9 (± 3.7)	48.8 (± 3.7)

 Table 3. Perioperative changes at baseline, before surgery, and 4 weeks following surgery for patients with gastrointestinal cancer undergoing emergency surgery at the University of Health and Welfare, Mita Hospital, Japan, 2016–2017

Values are expressed as mean  $\pm$  standard error.

\*Significant difference compared with the 4 weeks after surgery for multiple comparisons, <sup>†</sup>Significant interaction effect, n.s.: not significant.

6MWT: 6-min walk test; HADS: Hospital Anxiety and Depression Scale; SF36: 16-Item Short-Form Health Survey.

Table 4.	Change ratio for outc	omes at baselin	ne and 4 we	eks following s	urgery for patients	with gastroint	testinal cancer
	undergoing emergenc	y surgery at the	e University	of Health and	Welfare, Mita Hos	oital, Japan, 20	016-2017

Parameters	Improvement group (n=16)	Maintenance group (n=10)	Deterioration group (n=7)
6MWT	100.2 (± 12.1) *	93.2 (± 6.1)	84.1 (± 10.7)
SF36 subscales – Social function	84.0 (± 18.7)	106.5 (± 32.1)	98.6 (± 46.6)

Change ratios are expressed as mean  $\pm$  standard deviation.

\*Significant difference compared with the deterioration group, n.s.: not significant.

6MWT: 6-min walk test; SF36: 16-Item Short-Form Health Survey version 2.

constructed for exercise only as compared to the cancer prehabilitation proposed by Silver<sup>18, 19)</sup>. However, if it can improve the exercise capacity of patients with gastrointestinal cancer prior to surgery, it may be effective in preventing low exercise capacity following surgery in the same way as cancer prehabilitation. Additionally, as one of the possibilities, the information during surgery such as degree of blood transfusion may lead to the increasing postoperative exercise capacity because it relating the skeletal muscle and entire interlocking lung–heart–vascular oxygen transport system<sup>29)</sup>.

Therefore, this study demonstrates that pre-operative physical rehabilitation for patients with gastrointestinal cancer may be effective in reducing the decline in exercise capacity following surgery in the Japanese acute care center. Future studies should modify pre-operative physical rehabilitation into a multi-model intervention to address postoperative adverse events in a wider range of patients with gastrointestinal cancer.

This study has some limitations. First, the database used consisted of arbitrary samples from a small number of patients at a single center; thus, it cannot generalize the results of this study to other settings. In the future, these findings should be confirmed using a larger number of patients from multiple institutions. Second, only 6MWT was employed during the evaluation. Ideally, other parameters of exercise capacity, such as muscle strength, flexibility, and balance function, should be serially evaluated. Third, the performance of pre-operative physical rehabilitation was self-reported and thus participant to bias. In the future, the performance status of pre-operative physical rehabilitation should be objectively assessed.

In conclusions, improved exercise capacity by rehabilitation training prior to surgery leads to the preservation of physical function in surgical patients with gastrointestinal cancer. However, the factors causing this change remain unknown.

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#### Conflict of interest

The authors declare no conflict of interest.

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