

Original Article

# Factors that affect early postoperative health-related quality of life in patients with gastrointestinal cancer: a three-center cohort study

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**Abstract.** [Purpose] In this study, we investigated the preoperative and early postoperative health-related quality of life in patients who underwent surgical treatment for gastrointestinal cancer and also the factors that affect postoperative health-related quality of life. [Participants and Methods] The study included 198 patients who underwent elective surgery for gastrointestinal cancer (129 males and 69 females, age:  $65.4 \pm 11.8$  years). Health-related quality of life was evaluated using the Short-Form 36-Item Health Survey version 2 at the following time points: 1–2 days preoperatively (baseline) and 4 weeks postoperatively. [Results] Compared with baseline levels, physical functioning, bodily pain, vitality, as well as physical, social, and emotional role functioning significantly decreased 4 weeks postoperatively. In contrast, compared with baseline levels, mental health significantly improved 4 weeks postoperatively. Physical functioning and general health evaluated 4 weeks postoperatively were significantly associated with income, baseline health-related quality of life, and the 6-minute walk test. [Conclusion] It is important to consider baseline income and health-related quality of life and increase postoperative exercise capacity to improve health-related quality of life in patients who undergo surgical treatment for gastrointestinal cancer.

**Key words:** Gastrointestinal cancer, Health-related quality of life, Exercise capacity

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## INTRODUCTION

Globally, the number of gastrointestinal cancer (GIC) survivors is growing<sup>1)</sup>. However, a survivor may have decreased health-related quality of life (HRQOL) due to GIC itself or its treatment<sup>2)</sup>. In particular, treatment of GIC can cause not only postoperative general symptoms, such as pain and fatigue, but can also have a negative impact on daily physical activities<sup>3,4)</sup>. Additionally, the diagnosis of GIC can have a strong psychological impact on emotional function, such as inducing fear of illness and death<sup>4)</sup>. Therefore, improving early postoperative HRQOL of patients with GIC is important because of obvious need of a good clinical course after surgery.

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Previous research on the HRQOL of patients with GIC has generally investigated clinical and social characteristics as influencing factors<sup>5-14</sup>), and most of these studies have focused on patients undergoing surgical treatment<sup>6-10</sup>). However, longitudinal research on the HRQOL of perioperative patients with GIC is scarce<sup>7, 10</sup>), and there is also limited knowledge regarding the differences in HRQOL between the early phase after surgery and the preoperative phase. The longitudinal research that has been conducted on HRQOL in the perioperative phase<sup>7, 10</sup>) has only been performed in the form of single-center cohort studies, which limits the generalizability of the findings. Additionally, in our previous single-center cohort study<sup>15</sup>), the most influencing factor for HRQOL in patients with GIC was four weeks of exercise after surgery. However, a multi-center cohort study on the HRQOL of perioperative patients with GIC reveals the possibility of a change in factors influencing HRQOL because of likely differences in influencing factors in GIC patients with different residential areas.

Consequently, we hypothesize that the influencing factors of the HRQOL in patients with GIC may differ in a multi-center cohort study. This study aimed to investigate three acute medical institutions in Japan to determine whether physical function, perioperative management, clinical data, and social characteristics influence the early postoperative HRQOL of patients with GIC.

## PARTICIPANTS AND METHODS

The participants were all patients who were scheduled to undergo elective surgery for GIC or suspected GIC between March 1, 2016, and March 31, 2020, at three hospitals: the International University of Health and Welfare Mita Hospital, Tokyo, Japan, the International University of Health and Welfare Hospital, Tochigi, Japan, and the International University of Health and Welfare Ichikawa Hospital, Chiba, Japan. Exclusion criteria were a diagnosis of dementia at baseline, diagnosis of non-malignant tumor after surgery, heavy impact postoperative complications rated grade III or higher in the Clavien-Dindo classification<sup>16</sup>), and transfer to another hospital. This study was approved by the Research Ethics Board of the International University of Health and Welfare, Otawara-shi, Tochigi, Japan (registration number: 17-Io-202-2). All participants provided written and verbal informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

This was a cohort study conducted across three institutions. Each patient's HRQOL was evaluated at baseline (1–2 days before surgery) and four weeks after surgery. Potential influencing factors for HRQOL were assessed from baseline to four weeks after surgery. Each participant's perioperative care was managed by a surgeon who specialized in gastrointestinal surgery; the care provided was based on the clinical pathway for GIC surgery applied at each acute medical institution.

HRQOL was evaluated using the Japanese 36-Item Short-Form Health Survey (SF-36) version 2, acute form<sup>9, 11, 14</sup>). The SF-36 is a self-administered questionnaire that comprises eight subscales: physical functioning, physical role functioning, bodily pain, general health, vitality, social role functioning, emotional role functioning, and mental health. Scores for each subscale were calculated using the SF-36 version 2 scoring program recommended by iHope International<sup>17</sup>). For this study, each subscale score ranged from 0 to 100 points, with higher scores indicating better HRQOL. The patients completed the SF-36 at baseline and four weeks after surgery. The patients received instructions from rehabilitation staff regarding the response method for the SF-36, after which the patients completed the questionnaire. For physical functioning and general health, the patients were allocated to a high- or low-score group based on their score for that subscale four weeks after surgery because these subscales were related to the survival rate of cancer patients<sup>18</sup>) and the overall quality of life<sup>19</sup>). The patients who scored higher than the average score for the general Japanese population for the corresponding subscale<sup>17</sup>) were allocated to the high-score group, while those who scored lower than the average score for the general Japanese population for the corresponding subscale were allocated to the low-score group.

As potential factors that may influence HRQOL, we adopted the following four items based on previous studies: the postoperative complications<sup>10</sup>), body mass index<sup>14</sup>), exercise capacity<sup>8, 13</sup>), and clinical characteristics of patients<sup>1, 5-7, 9-12</sup>).

Postoperative complications among the patients were examined by consulting their medical records four weeks after surgery, and were graded using the Clavien-Dindo classification<sup>16</sup>). The complications of grades III and IV on the Clavien-Dindo classification were not included because these were part of the exclusion criteria.

Each patient's body mass index was calculated using weight (measured while wearing clothes) and height; this evaluation was performed at two time points: baseline and four weeks after surgery.

Exercise capacity was evaluated using the six-minute walk test (6MWT). To administer this test, we applied the associated guidelines of the American Thoracic Society<sup>20</sup>). Specifically, patients were instructed to walk back and forth along a 30-meter hallway for six minutes at a pace that would cause them to exert maximum effort throughout the walk. In this study, the total distance covered in six minutes was recorded in meters.

Furthermore, the following age at baseline, gender, clinical stage of cancer after surgery, comorbidities (hypertension, hyperlipidemia, diabetes mellitus, cardiac diseases, respiratory diseases, orthopedic diseases, and/or cerebrovascular diseases), neoadjuvant therapy, diagnosis, type of surgery received (open surgery, laparoscopic surgery, or robot-assisted surgery), income, employment status, and living with a spouse were incorporated as potential factors influencing HRQOL following the results of previous studies<sup>5-7, 9-12, 14</sup>).

For each of the eight SF-36 subscales, the scores at baseline and four weeks after surgery were compared using paired *t*-tests. The associations between the factors potentially influencing HRQOL and each pair of participant groups (the high-score

and low-score groups) for the two SF-36 subscales (physical functioning and general health) were also examined. Clinical characteristics (i.e., age, body mass index, 6MWT, and baseline SF-36 subscale scores) were analyzed using an unpaired t-test, while categorical variables (i.e., gender, clinical cancer stage, comorbidities, and diagnosis) were analyzed using  $\chi^2$  tests. Furthermore, the relationship between physical functioning and general health four weeks after surgery and factors found to be related were analyzed using logistic regression analysis. The high and low scores for each of the SF-36 subscales four weeks after surgery were set as dependent variables, and the factors significantly related to a high or low score for each SF-36 subscale four weeks after surgery were set as independent variables. All statistical analyses were performed using SPSS (version 24.0; SPSS Inc., Chicago, IL, USA). Statistical significance was set at  $p < 0.05$ .

## RESULTS

A total of 503 patients were approached for participation in this research. Of these, 45 declined to participate, and 260 were excluded (61 met exclusion criteria, and 199 provided incomplete data). Thus, 198 patients (129 males and 69 females; age:  $65.4 \pm 11.8$  years) were ultimately enrolled in the study.

Table 1 shows the perioperative changes in the SF-36 subscale scores along with the average scores of the general Japanese population for each of these subscales<sup>17</sup>. At four weeks after surgery, the scores for physical functioning, physical role functioning, bodily pain, vitality, social role functioning, and emotional role functioning were significantly lower than the corresponding scores at baseline. Conversely, scores for mental health were significantly higher four weeks after surgery when compared with the scores at baseline. Moreover, four weeks after surgery, the only subscale for which the patients' mean score exceeded that of the general Japanese population was the mental health subscale.

The relationships between the study variables and the high- and low-score groups for physical functioning and general health four weeks after surgery are shown in Tables 2 and 3. Many relations were significant, but gender, clinical cancer stage, diagnosis, body mass index, and living with a spouse were not significantly related.

The logistic regression analysis showed that 6MWT at four weeks after surgery ( $\beta=0.012$ ,  $p$ -value=0.000, Odds ratio (OR)=1.012, 95% confidence interval (95% CI)=1.008–1.017) and vitality at baseline ( $\beta=0.033$ ,  $p$ -value=0.001, OR=1.033, 95% CI=1.014–1.053) were significantly associated with physical functioning at four weeks after surgery ( $\chi^2=58.008$ ,  $p$ -value for  $\chi^2$  test=0.000,  $p$ -value for Hosmer–Lemeshow test=0.918). 6MWT at four weeks after surgery ( $\beta=0.006$ ,  $p$ -value=0.003, OR=1.006, 95% CI=1.002–1.010), low income ( $\beta=-2.188$ ,  $p$ -value=0.006, OR=0.112, 95% CI=0.023–0.537), and general health at baseline ( $\beta=0.081$ ,  $p$ -value=0.000, OR=1.084, 95% CI=1.053–1.116) were significantly associated with general health at four weeks after surgery ( $\chi^2=69.931$ ;  $p$ -value for  $\chi^2$  test=0.000;  $p$ -value for Hosmer–Lemeshow test=0.480). The most frequently identified factor influencing physical functioning and general health at four weeks after surgery was the 6MWT at four weeks after surgery.

## DISCUSSION

Among our sample, in the early postoperative period, the patients' scores for all SF-36 subscales except general and mental health were significantly lower than the corresponding scores at baseline (Table 1). A previous study that investigated the HRQOL of patients with GIC before surgery and at six weeks after discharge reported that the scores for emotional function were significantly lower at six weeks after discharge when compared to the scores recorded before surgery<sup>10</sup>. Conversely, in the present study, which examined postoperative HRQOL at an earlier stage (i.e., four weeks post-surgery), significantly lower scores were observed in terms of not only a mental component (vitality), but also physical (physical functioning and bodily pain) and social role components (physical role functioning, social role functioning, and emotional role functioning).

**Table 1.** Changes in scores for the Short-Form 36-Item subscales between baseline and four weeks after surgery

	Baseline	Four weeks after surgery	Average score for the general Japanese population <sup>17</sup> )
SF-36 subscales			
Physical functioning	86.7 ± 14.6	80.1 ± 17.7*	87.6 ± 15.7
Physical role functioning	79.6 ± 24.2	65.6 ± 28.0*	86.9 ± 19.7
Bodily pain	82.6 ± 21.7	68.6 ± 22.6*	73.6 ± 23.1
General health	59.8 ± 15.7	60.8 ± 16.7	63.7 ± 18.7
Vitality	68.0 ± 19.2	64.6 ± 20.5*	64.7 ± 19.6
Social role functioning	81.6 ± 21.5	72.3 ± 28.1*	84.3 ± 20.5
Emotional role functioning	80.2 ± 23.6	73.4 ± 28.5*	86.4 ± 20.6
Mental health	68.6 ± 20.7	72.9 ± 18.7*	71.2 ± 18.8

Values are means ± standard deviations. \*Significant difference for paired t-tests. SF-36: Short-Form 36-Item.

**Table 2.** Influence of patients' clinical characteristics on the high- and low-score groups for physical functioning and general health of the Short-Form 36-Item at four weeks after surgery

	All patients n=198	Patients with gastrointestinal cancer			
		Physical functioning		General health	
		High n=91	Low n=107	High n=72	Low n=126
Age	65.4 ± 11.8	63.3 ± 11.3	67.3 ± 12.0*	63.2 ± 14.3	66.7 ± 10.0*
Gender (male)	129 (65)	61 (67)	68 (64)	43 (60)	86 (68)
Clinical cancer stage					
I	76 (38)	40 (44)	36 (34)	32 (44)	44 (35)
II	55 (28)	22 (24)	33 (31)	19 (26)	36 (29)
III	44 (22)	22 (24)	22 (21)	17 (24)	27 (21)
IV	23 (12)	7 (8)	16 (15)	4 (6)	19 (15)
Comorbidities					
Hypertension	60 (30)	21 (23)	39 (36) †	23 (32)	37 (29)
Hyperlipidemia	15 (8)	5 (5)	10 (9)	5 (7)	10 (8)
Diabetes mellitus	31 (16)	12 (13)	19 (18)	8 (11)	23 (18)
Cardiac diseases	19 (10)	8 (9)	11 (10)	4 (6)	15 (12)
Respiratory diseases	11 (6)	4 (4)	7 (7)	4 (6)	7 (6)
Orthopedic diseases	17 (9)	4 (4)	13 (12)	6 (8)	11 (9)
Cerebrovascular diseases	9 (5)	0 (0)	9 (8) †	6 (8)	3 (2)
Diagnosis					
Esophageal cancer	6 (3)	2 (2)	4 (4)	1 (1)	5 (4)
Gastric cancer	46 (23)	22 (24)	24 (22)	19 (26)	27 (21)
Liver cancer	22 (11)	9 (10)	13 (12)	5 (7)	17 (13)
Gallbladder cancer	3 (2)	0 (0)	3 (3)	0 (0)	3 (2)
Bile duct cancer	1 (1)	0 (0)	1 (1)	0 (0)	1 (1)
Pancreatic cancer	14 (7)	3 (3)	11 (10)	4 (6)	10 (8)
Colon cancer	60 (30)	31 (34)	29 (27)	23 (32)	37 (29)
Rectal cancer	46 (23)	24 (26)	22 (21)	20 (28)	26 (21)
Received neoadjuvant therapy	8 (4)	0 (0)	8 (7) †	0 (0)	8 (6)
Surgery type					
Open surgery	52 (26)	12 (13)	40 (37) †	11 (15)	41 (33) †
Laparoscopic surgery	139 (70)	72 (79)	67 (63) †	59 (82)	80 (63) †
Robot-assisted surgery	7 (4)	7 (8)	0 (0) †	2 (3)	5 (4)
Clavien–Dindo classification‡					
Grade I	40 (20)	18 (20)	25 (23)	12 (17)	31 (25)
Grade II	43 (22)	10 (11)	30 (28) †	9 (13)	31 (25) †
Length of hospital stay	18.2 ± 10.3	16.4 ± 9.2	19.7 ± 11.0*	15.8 ± 7.6	19.5 ± 11.4*

Values are numbers (%) or means ± standard deviations. \*Significant difference for unpaired t-tests. †Significant difference for  $\chi^2$  tests. ‡Includes duplicate cases.

This indicates that, in future examinations of the HRQOL of perioperative patients with GIC, measurements should be performed relatively soon after surgery. Additionally, for the present sample, the only HRQOL element that significantly improved four weeks after surgery was mental health (Table 1). The mental health subscale of the SF-36 is part of the questionnaire's "mental component summary" dimension, which also includes vitality, social role functioning, and emotional role functioning<sup>17</sup>). Japanese patients with GIC may experience unique changes in HRQOL across the perioperative period.

The most frequently identified influencing factor for HRQOL four weeks after surgery was 6MWT at four weeks after surgery. Associations between 6MWT performance and HRQOL in patients with GIC have previously been reported<sup>8, 13</sup>). Moreover, as mentioned previously, the improvement or maintenance of exercise capacity may prevent the decreasing early postoperative HRQOL in patients with GIC. However, the mechanism by which the improvement in exercise capacity of patients with GIC relates to HRQOL remains unclear. Previous studies suggest that fatigue of cancer survivors acts as a

**Table 3.** Influence of patients' physical function and social information on the high- and low-score groups for physical functioning and general health of the Short-Form 36-Item at four weeks after surgery

	All patients n=198	Patients with gastrointestinal cancer			
		Physical functioning		General health	
		High n=91	Low n=107	High n=72	Low n=126
Body mass index					
Baseline	23.5 ± 3.7	23.3 ± 3.9	23.7 ± 3.5	23.5 ± 3.6	23.6 ± 3.8
Four weeks after surgery	22.5 ± 3.6	22.4 ± 3.5	22.6 ± 3.7	22.5 ± 3.5	22.5 ± 3.7
Six-minute walk test					
Baseline	509.8 ± 101.5	534.6 ± 81.7	488.6 ± 111.8	535.5 ± 89.8	495.0 ± 105.1*
Four weeks after surgery	500.4 ± 103.3	549.0 ± 80.6	459.0 ± 102.7	537.1 ± 91.7	479.4 ± 104.0*
Income					
High	59 (30)	30 (33)	29 (27)	24 (33)	35 (28)
Middle	112 (57)	51 (56)	61 (57)	46 (64)	66 (52)
Low	27 (14)	10 (11)	17 (16)	2 (3)	25 (20) †
Employment status (employed)	92 (46)	51 (56)	41 (38) †	42 (58)	50 (40) †
Living with spouse (yes)	136 (69)	69 (76)	67 (63)	54 (75)	82 (65)
SF-36 subscales at baseline					
Physical functioning	86.7 ± 14.6	92.7 ± 7.9	81.6 ± 16.9*	90.9 ± 10.3	84.3 ± 16.1*
Physical role functioning	79.6 ± 24.2	84.7 ± 18.9	75.2 ± 27.3*	85.8 ± 19.5	76.0 ± 25.9*
Bodily pain	82.6 ± 21.7	86.0 ± 18.9	79.6 ± 23.5*	86.1 ± 19.9	80.5 ± 22.5
General health	59.8 ± 15.7	63.2 ± 15.1	56.9 ± 15.6*	69.2 ± 13.0	54.4 ± 14.6*
Vitality	68.0 ± 19.2	73.9 ± 18.0	62.9 ± 18.7*	75.9 ± 17.3	63.4 ± 18.7*
Social role functioning	81.6 ± 21.5	86.8 ± 18.9	77.2 ± 22.7*	86.6 ± 19.6	78.8 ± 22.1*
Emotional role functioning	80.2 ± 23.6	85.9 ± 16.8	75.4 ± 27.3*	87.3 ± 17.0	76.2 ± 25.8*
Mental health	68.6 ± 20.7	73.4 ± 18.7	64.6 ± 21.6*	76.9 ± 17.5	63.8 ± 20.9*

Values are numbers (%) or means ± standard deviations. \*Significant difference for unpaired t-tests. †Significant difference for  $\chi^2$  tests. SF-36: Short-Form 36-Item.

mediator between physical fitness and quality of life<sup>21</sup>). In the future, the relationship between exercise capacity and HRQOL in patients with GIC, considering postoperative metabolic dynamics, should be investigated.

The second most important factor impacting HRQOL four weeks after surgery was HRQOL at baseline, specifically, vitality and general health. A previous review reported that low HRQOL at an early time point in a study (i.e., baseline) is associated with low HRQOL at later time points during study follow-up (from post-treatment to postdiagnosis)<sup>22</sup>). Additionally, a previous study of perioperative patients with GIC found preoperative HRQOL to be associated with HRQOL six weeks after discharge<sup>10</sup>). Thus, increasing the preoperative HRQOL of patients with GIC may result in improved or consistent early postoperative HRQOL.

Regarding social characteristics influencing the HRQOL of patients with GIC, income at baseline<sup>9, 12</sup>) was found to be significantly associated. Japanese patients with GIC are guaranteed medical care by Japan's national health insurance system; however, it appears that Japanese patients nevertheless have similar income concerns to patients in other countries where the national health insurance system is not as substantial<sup>9, 12</sup>).

This study has some limitations. First, all the examined patients did not have the same surgical site or undergo the same type of surgery. Ideally, a multi-center cohort study for examining changes in early postoperative HRQOL should feature a homogenous group of patients with GIC. Second, the emotional function was not evaluated during the perioperative period. Psychological function measures, such as the Hospital Anxiety and Depression Scale and the Geriatric Depression Scale-15, should be administered at several time points over the perioperative period. Third, the patients' engagement in physical activity from discharge to four weeks after surgery was unclear and may be subject to self-report bias. In future studies, physical activity after discharge should be directly monitored.

In the conclusion, early after surgery, scores for most HRQOL items decrease significantly, with only scores for mental health significantly improving. To increase early postoperative HRQOL in surgical patients with GIC, it may be necessary to consider an increase in post-surgery exercise capacity as in previous single-center cohort study<sup>15</sup>). In the future, patients with GIC will need an insurance system that can sustain long-term physical rehabilitation.

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## Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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