doi: 10.2490/prm.20210001 Progress in Rehabilitation Medicine 2021; Vol. 6, 20210001

ORIGINAL ARTICLE

Preoperative Improvement in Physical Function by Comprehensive Rehabilitation Leads to Decreased Postoperative Complications in Gastrointestinal Cancer Patients

Tsuyoshi Hara, RPT, PhD [a] Eisuke Kogure, RPT, PhD [b] Akira Kubo, RPT, PhD [a] and Wataru Kakuda, MD, PhD [c]

Objectives: The aim of this study was to investigate how baseline laboratory data and changes in physical function due to preoperative rehabilitation training in gastrointestinal cancer (GIC) patients can influence the frequency of postoperative complications (PCs). **Methods:** We enrolled 45 patients who were scheduled for elective surgery for GIC (27 men and 18 women, mean age 63.6±9.5 years). All patients underwent a medical examination and received general instruction from a rehabilitation physician and exercise instruction from a physical therapist from 7 to 34 days before the surgery. PCs were graded using the Clavien-Dindo classification based on the medical records 1 month postoperatively. We measured the grip strength and the isometric knee extension torque and conducted the 6-min walk test (6MWT) at baseline and just before surgery. The surgical duration, blood loss, and blood transfusion data were collected. Baseline laboratory information, including C-reactive protein levels, serum albumin levels, platelet count, white blood cell count, and the estimated glomerular filtration rate, was recorded. **Results:** The frequency of PCs was negatively correlated to the change in the 6MWT (β=−0.36) and positively correlated to the surgical duration (β=0.41). Baseline albumin was positively correlated to the change in the 6MWT distance (β=0.35). This model demonstrated an acceptable fit to the data (goodness of fit index=0.980, comparative fit index=1.000, root mean square error of approximation=0.000). **Conclusions:** The improvement of gait ability achieved with preoperative rehabilitation training in patients undergoing elective GIC surgery led to decreased PCs.

Key Words: physical therapists; preoperative rehabilitation; 6-min walk test

INTRODUCTION

Postoperative complications (PCs) in gastrointestinal cancer (GIC) patients are not only a physical and mental burden but also lead to a reduced quality of life[1)] and lifespan.[2)] In previous studies, exercise-related factors, including physical function[3,4)] and body composition,[5–9)] have been linked to PCs in GIC patients. The PCs affected by exercise-related factors in previous studies[3–9)] included anastomotic leakage, pancreatic fistula, bleeding, wound infection, intraabdominal infection, ileus, postoperative acute respiratory failure, and pneumonia. A systematic review of major abdominal surgery reported that preoperative physical exercise may lead to a reduction of postoperative pulmonary complications and postoperative overall morbidity.[10)] These findings suggest that a preoperative improvement in exercise-related factors in GIC patients can reduce PCs. However, patient demographics (age at baseline, sex, clinical stage of cancer after surgery, and comorbidities),[5–7)] surgical information

Received: October 2, 2020, Accepted: December 16, 2020, Published online: January 8, 2021
[a] Department of Physical Therapy, School of Health Science, International University of Health and Welfare, Tochigi, Japan
[b] Rehabilitation Progress Center Incorporated, Tokyo, Japan
[c] Department of Rehabilitation Medicine, School of Medicine, International University of Health and Welfare, Chiba, Japan
Correspondence: Tsuyoshi Hara, RPT, PhD, 2600-1 Kitakanemaru, Otawara-shi, Tochigi 324-8501, Japan, E-mail: hara@iuhw.ac.jp

(type of surgery, surgery duration, blood loss, and blood transfusion),[5,6,11–13] and laboratory data [serum albumin (Alb), platelet count, white blood cell count, and estimated glomerular filtration rate][14–18] have also been reported as important factors related to PCs in GIC patients. Therefore, the ability of exercise intervention to decrease PCs in GIC patients should be examined in an analysis that also includes these other factors.

The aim of this study was to investigate how preoperative changes in physical function due to rehabilitation training in GIC patients can influence the frequency of PCs and to examine the relationship between such changes in physical function and baseline laboratory data.

MATERIALS AND METHODS

Subjects

The study was approved by the Research Ethics Board of the International University Health and Welfare Mita Hospital, Minato-ku, Tokyo, Japan, and study procedures were carried out in accordance with ethical standards (registration: 5–16-2). Moreover, all patients provided written and oral informed consent, and the study was conducted according to the principles of the Declaration of Helsinki. All patients were scheduled for elective surgery for GIC or suspected GIC at the International University Health and Welfare Mita Hospital, which is an accredited Tokyo-designated cancer treatment hospital, between March 1, 2016, and December 31, 2017. Exclusion criteria included the rehabilitation physician's decision that preoperative physical rehabilitation would adversely affect the patient's medical condition (e.g., in patients with bone metastasis), a history of preoperative orthopedic or cerebrovascular disease that could affect activities of daily living, and the tumor being diagnosed as non-malignant after surgery. The following clinical data were collected: intervention days, intervention period, exercise rate, and the length of hospital stay.

Study Design

This was a cross-sectional study of patients from a single center. The presence of PCs was recorded based on the medical records 1 month postoperatively, and the changes in exercise-related factors between baseline values and those just before surgery were recorded in patients who underwent preoperative physical rehabilitation. We also recorded demographic, surgical, and laboratory data. Perioperative care for all subjects was managed by the gastrointestinal surgeon based on the clinical protocols of the International University Health and Welfare Mita Hospital. The standard postoperative rehabilitation program for all subjects included aerobic and resistance exercise based on the clinical protocols of the International University Health and Welfare Mita Hospital provided by a physical therapist and performed for 20 to 40 min in the ward or rehabilitation room according to the subject's clinical course. The PCs were graded using the Clavien-Dindo classification[19] based on the medical records 1 month postoperatively. In this study, Clavien-Dindo classification grade II or higher was defined as a postoperative complication.[15]

Preoperative Physical Rehabilitation

All patients underwent a medical examination and patient education from a rehabilitation physician and exercise instruction from a physical therapist. The rehabilitation physician performed medical examinations to assess each patient's general condition and factors that might affect the preoperative physical rehabilitation. Additionally, the patients were instructed to achieve a daily protein intake based on the European Society for Clinical Nutrition and Metabolism guidelines.[20] Direct exercise instruction was given to all patients in a 1-h session by a physical therapist. The exercise program consisted of up to 50 min of unsupervised home-based exercise, alternating between aerobic and resistance exercises. The exercise program included a 5-min warm-up, 20 min of aerobic exercise, 20 min of resistance exercise, and a 5-min cooldown. Examples of the aerobic exercise included walking, jogging, swimming, or cycling, at the patient's discretion and starting at 50% of the heart rate reserve. Examples of resistance exercise included squats and training of inspiratory muscles. The frequency of preoperative physical rehabilitation for all GIC patients was set at one session per day for three or more days per week. Additionally, all patients were given a record book in which to record the completion of their exercises. The exercise program was determined with reference to previous studies.[21,22]

Evaluation of Exercise-related Factors

We analyzed the grip strength (GS), the isometric knee extension torque (IKET), and the 6-min walk test (6MWT) distance of each patient. GS was measured twice with maximum effort for both hands. We used the product of the maximum left and right values for our evaluations. IKET was evaluated using the isometric test mechanism of the HUR 5530 leg extension/curl rehab machine (HUR Ltd, Kokkola, Finland). The patient was instructed to extend their right knee against the pad with maximum effort for 5 s while in the sitting position. We used the normalized joint torque calculated from the maximum force and the distance from the knee joint space to the pad center normalized by body weight. The 6MWT distance was evaluated based on the guidelines of the American Thoracic Society.[23] Patients were instructed to walk back and forth along a 50-m hallway for 6 min at a pace that would require maximum effort by the end of the walk. In this study, the total distance covered in 6 min was recorded in meters. Each parameter of the exercise-related factors was calculated as the change from baseline (prior to the rehabilitation program) to just before surgery.

Other PC Factors

Body composition data, including body mass index (BMI), skeletal muscle index (SMI), and visceral fat area (VFA), were recorded at baseline.[5–9] BMI was calculated using the height and weight measured with the patient clothed. SMI and VFA were evaluated from a computed tomography (CT) image at the third lumbar vertebra (L3) using thresholds of −29 to +150 Hounsfield units for skeletal muscle and −150 to −50 Hounsfield units for visceral adipose tissue (water was defined as 0, air as 1000 Hounsfield units).[24] SMI was normalized using the sum of the cross-sectional areas (cm^2) of multiple muscles (including the psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal oblique abdominals, and the rectus abdominis muscles) divided by the square of the height (cm^2/m^2). VFA was recorded as the cross-sectional area (cm^2) of visceral fat. SMI and VFA analyses were performed using ImageJ version 1.51 (NIH, Bethesda, MD, USA) (Java 1.8.0_112) by one analyst.

The following clinical data[5–7,11–18] were collected: age at baseline, sex, clinical stage of cancer after surgery, comorbidities (hypertension, hyperlipidemia, diabetes mellitus, cardiac diseases, and respiratory diseases), diagnosis, type of surgery (laparoscopic or open), surgery duration, blood loss, blood transfusion (red cell concentrates and fresh frozen plasma), baseline laboratory data (Alb, platelet count, white blood cell count, estimated glomerular filtration rate, and C-reactive protein), and baseline percent forced expiratory volume in 1 s.

Statistical Analysis

The unpaired *t*-test was used for comparisons of the clinical characteristics between patients with and without complications. Categorical variables and the frequency of PCs were compared using the chi-squared test. The relationships between the frequency of PCs and the related factors were analyzed using path analysis of structural equation model analysis. The initial model tested whether variables significantly associated with PCs were directly related to PCs. Baseline laboratory data were confirmed to be directly and/or indirectly related to PCs. This study derived a final model by excluding the non-significant variables identified in the initial model. The fits of all models were evaluated using the model chi-squared value [χ^2; low χ^2 relative to degrees of freedom (df) with no significant P-value], the goodness of fit index (GFI; values >0.95 indicate good model fit), the comparative fit index (CFI; values >0.95 indicate good model fit), and the root mean square error of approximation (RMSEA; values <0.07 indicate good model fit).[25] All statistical analyses were performed using SPSS statistics version 24.0 and SPSS Amos version 24.0 (SPSS Inc, Chicago, IL, USA). A P-value <0.05 was considered significant.

RESULTS

A total of 288 patients were approached for consent; 172 patients declined to participate, and 71 patients were excluded (45 due to exclusion criteria and 26 due to incomplete data). Finally, 45 patients were enrolled in the study (**Fig. 1**). Patients were divided into two groups based on the presence or absence of complications at 1 month postoperatively—14 and 31 patients were included in the complications and no complications groups, respectively. The frequencies of PCs, based on the Clavien-Dindo classification, in the complications group were as follows: grade I: 36%, grade II: 100%, grade III: 7%, and grade IV: 7%. However, in the no complication group, only grade I complications were observed, at 29%. There were no significant differences in the number of intervention days, the length of the intervention period, the exercise rate, or the length of hospital stay between the two groups (**Table 1**). No significant adverse events (such as the onset of new orthopedic diseases or cerebrovascular diseases) were observed during this study.

Factor Structure Model Leading to PCs

The baseline clinical characteristics of the two groups are shown in **Table 1**. The duration of surgery and the change in the 6MWT distance were significantly different between the groups. Our initial model determined that both the surgical duration and the change in the 6MWT distance were directly related to PCs, and that Alb was indirectly related to PCs. The surgical duration was significantly and positively correlated to PCs (standardized β=0.391, P <0.05), and the change in the 6MWT distance was significantly and nega-

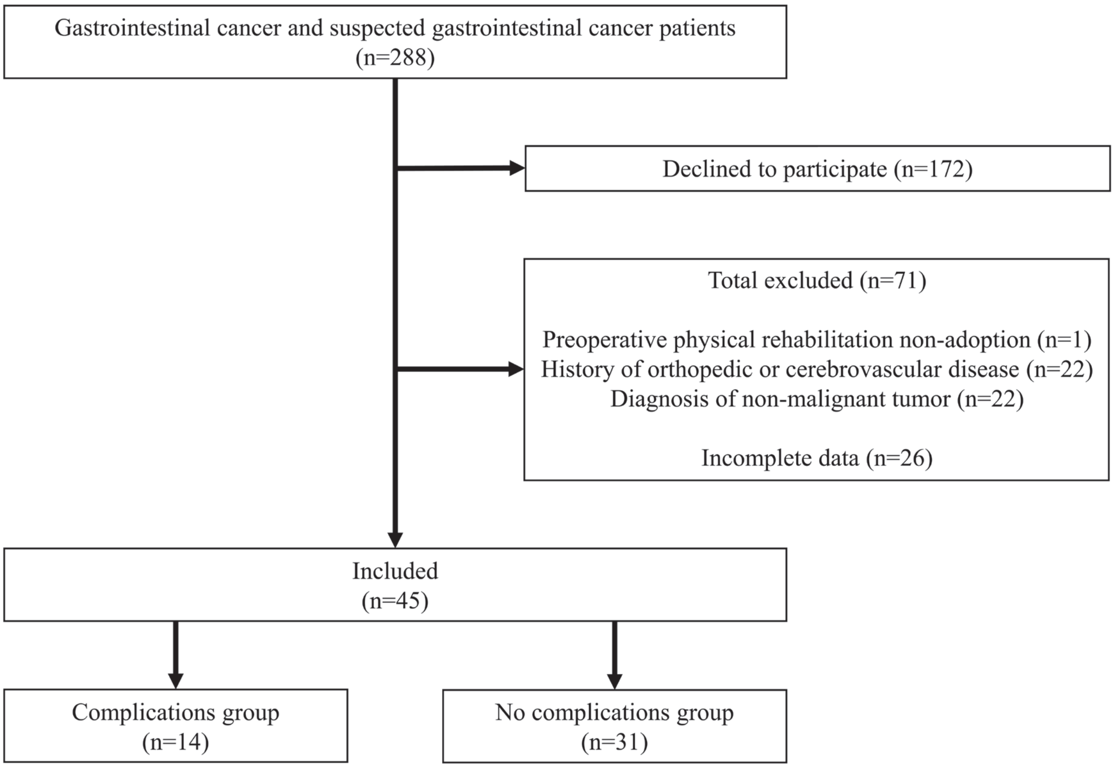

Fig. 1. Patient flow through the study.

tively correlated to PCs (standardized β=−0.355, P <0.05). Alb correlated significantly and positively with the change in the 6MWT distance (standardized β=0.343, P <0.05), but not with PCs. No other baseline laboratory parameter significantly correlated with PCs. The fit parameters of the initial model were: χ^2=26.606, df=11, P=0.01, GFI=0.891, CFI=0.523, RMSEA=0.180 (**Fig. 2**). In the final analysis, the surgical duration was significantly and positively correlated to PCs (standardized β=0.407, P <0.05), and the change in the 6MWT distance was significantly and negatively correlated to PCs (standardized β=−0.356, P <0.05) (**Table 2**). In the final model, Alb was negatively and indirectly correlated with PCs through the 6MWT (standardized β=−0.124, P <0.05) (**Table 2**) and significantly and positively correlated to the change in the 6MWT distance (standardized β=0.349, P <0.05). The fit parameters of the final model were: χ^2=1.839, df=3, P=0.61, GFI=0.980, CFI=1.000, RMSEA=0.000 (**Fig. 3**).

DISCUSSION

We found that PCs in GIC patients were significantly and positively correlated with the surgical duration and significantly and negatively correlated with the change in the 6MWT distance (**Table 2**, **Fig. 3**). Additionally, the impact of improving the 6MWT distance in GIC patients preoperatively was unclear because the baseline characteristics showed no significant differences (**Table 1**). In future studies, influential factors should be investigated, including the exclusion criteria in this study, to assess the improvement of gait ability in GIC patients before surgery.

Hanaoka et al. found that the degree of surgical stress, an extension of the surgical duration, was associated with PCs in GIC patients.[11] Under severe surgical stress, immune functions are increased to avoid tissue hypoxia in humans,[26] and cardiac output is increased to sustain life.[27] In GIC patients who are under severe stress because of prolonged surgery, the stress overwhelms the body's compensatory responses and complications occur.

In rehabilitation medicine, the 6MWT is a simple evaluation scale for cardiopulmonary reserve[23] that captures increased utilization of oxygen peripherally (in skeletal muscle) and improvements in the entire interlocking lung–heart–vascular oxygen transport system,[28] reflecting oxygen intake, carbon dioxide excretion, and pulmonary blood flow.[29] PCs are a result of multiorgan failure resulting from the body's inability to deliver adequate oxygen to the tissues.[29, 30] A

Table 1. Patient demographics, baseline characteristics, surgical parameters, gait improvement, and postoperative complications in 45 GIC patients who underwent elective surgery after preoperative rehabilitation

		Complications group (n=14)		No complications group (n=31)		P-value
Age (years)		66.9±6.1		62.1±10.4		0.121
Gender	Female	3	-21	15	-48	0.111
	Male	11	-79	16	-52	
Clinical stage of the cancer	I	5	-36	8	-26	0.502
	II	6	-43	9	-29	0.497
	III	3	-21	12	-39	0.321
	IV	0	0	2	-6	1
Comorbidities	Hypertension	5	-36	11	-35	1
	Hyperlipidemia	1	-7	3	-10	1
	Diabetes mellitus	1	-7	7	-23	0.402
	Cardiac disease	2	-14	3	-10	0.639
	Respiratory disease	1	-7	2	-6	1
Diagnosis	Esophageal cancer	2	-14	3	-10	0.639
	Gastric cancer	1	-7	1	-3	0.53
	Liver cancer	1	-7	5	-16	0.648
	Gallbladder cancer	1	-7	0	0	0.311
	Bile duct cancer	1	-7	3	-10	1
	Pancreatic cancer	5	-36	7	-23	0.47
	Colon cancer	2	-14	6	-19	1
	Rectal cancer	1	-7	6	-19	0.407
Neoadjuvant therapy		4	-29	4	-13	0.231
Type of surgery	Open	9	-64	17	-55	0.746
	Laparoscopic	5	-36	14	-45	
Surgery duration (min)		375.4±119.8		270.5±117.7		0.009*
Blood loss (ml)		538.6±617.2		336.2±575.7		0.291
Blood transfusion (ml)	Red cell concentrates	200.0±605.8		126.5±401.5		0.631
	Fresh frozen plasma	68.6±256.6		85.2±266.9		0.846
Laboratory data	Serum albumin (mg/dl)	4.3±0.3		4.5±0.3		0.122
	Platelets (10^3/µl)	23.8±8.6		21.2±7.5		0.312
	White blood cells (/µl)	5952.1±2291.8		5815.2±1606.9		0.818
	Estimated glomerular filtration rate (ml/min/1.73m^2)	71.0±13.0		79.0±15.9		0.108
	C-reactive protein (mg/dl)	0.2±0.2		0.3±0.5		0.946
Percent forced expiratory volume in 1 s at baseline (%)		78.3±8.2		78.7±6.5		0.884
Body mass index (kg/m^2)		21.9±2.7		23.7±3.7		0.112
Visceral fat area (cm^2)		77.6±48.9		90.4±75.2		0.565
Skeletal muscle index (cm^2/m^2)		35.9±9.0		36.3±8.9		0.876
Change in exercise factor (%)	Grip strength	100.1±6.1		98.6±7.1		0.498
	Isometric knee extension torque	101.2±17.7		105.6±26.0		0.564
	6MWT	96.6±6.3		102.8±9.0		0.026*

Table 1. (continued)

		Complications group (n=14)		No complications group (n=31)		P-value
Clavien-Dindo classification†	Grade I	5	-36	9	-29	
	Grade II	14	-100	0	0	
	Grade III	1	-7	0	0	
	Grade IV	1	-7	0	0	
	Grade V	0	0	0	0	
Postoperative complications						
	Infection	6				
	Ileus	2				
	Abscess	1				
	Anastomotic leakage	1				
	Heart failure	1				
	Delirium	1				
	Herpes zoster	1				
	Scabies	1				
	Wound infections opened at the bedside	3				
	Pleural effusion	3				
	Pancreatic fistula	2				
	Others	7				
Intervention days		8.6±7.3		10.0±7.4		0.56
Intervention period (days)		16.3±5.0		16.2±6.4		0.975
Exercise rate (%)		55.7±45.4		63.0±40.6		0.596
Length of hospital stay (days)		29.9±17.6		21.7±14.7		0.109

Values are numbers (%) or mean ± standard deviation.
* Analyzed by unpaired *t*-test.
† Includes duplicate cases, compared with grades 0, I, and II or higher.
6MWT, 6-min walk test.

high preoperative cardiopulmonary reserve can help patients adapt to the oxygen requirements caused by surgical stress in the perioperative period. Therefore, GIC patients who were able to improve their 6MWT distance before surgery had a decreased risk of PCs. Consequently, preoperative physical rehabilitation is recommended for GIC patients. However, in this study, the improvement in cardiopulmonary reserve after preoperative physical rehabilitation was not evaluated directly. In future studies, the maximum oxygen consumption of GIC patients should be measured using an exercise tolerance test.

In this study, baseline serum albumin levels significantly and positively correlated with the change in 6MWT distance (**Fig. 3**). The albumin synthesis rate in skeletal muscle increases after aerobic exercise regardless of age.[31] Protein synthesis by skeletal muscles is important for recovery from oxidative stress after aerobic exercise. Serum albumin is an important factor for increasing exercise capacity by preoperative physical rehabilitation in GIC patients who are not at high risk for malnutrition (Alb <3.5 mg/dl).[14] Therefore, a nutritional approach, for example by consuming adequate protein as instructed in this study, is an important factor in the improvement of gait ability in GIC patients. To achieve a preoperative increase of physical function in GIC patients, comprehensive rehabilitation requires physical exercise and a nutritional approach.

This study has some limitations. First, the results cannot be generalized because this a single medical center study with a small number of patients, resulting in a selection bias of GIC patients, such as those in a good condition with high

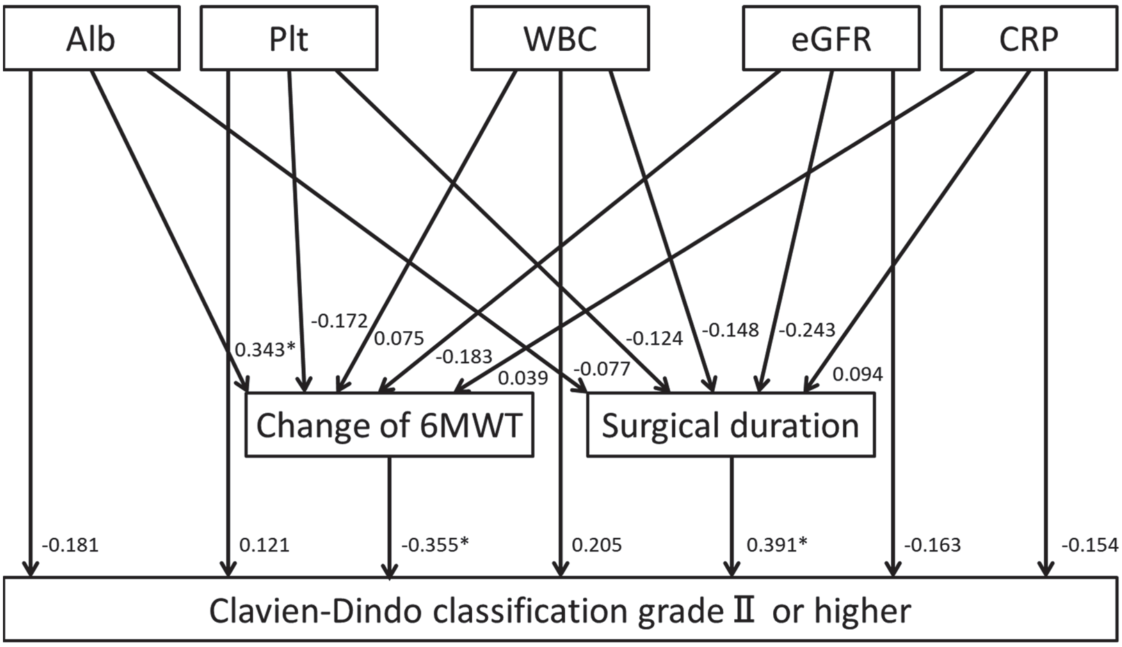

Fig. 2. Initial model of factors leading to postoperative complications (PCs) in patients with gastrointestinal cancer. For the variables shown in the figure, the path coefficients are standardized and the error variables are omitted. Laboratory values [serum albumin (Alb), platelet count (Plt), white blood cell count (WBC), estimated glomerular filtration rate (eGFR), and C-reactive protein (CRP)] were analyzed for their correlation with PCs, changes in the 6-min walk test (6MWT) distance, and surgical duration. The correlation of changes in 6MWT distance and surgical duration with PCs were also analyzed. Significant positive correlations were found between serum albumin and changes in 6MWT and between the surgical duration and PCs. A significant negative correlation was found between changes in the 6MWT distance and PCs. Model fit: χ^2=26.606, degrees of freedom=11, P=0.01, goodness of fit index (GFI)=0.891, comparative fit index (CFI)=0.523, root mean square error of approximation (RMSEA)=0.180, *P <0.05.

Table 2. Correlation of each variable with postoperative complications in the final model

	Standardized direct effect	Standardized indirect effect	Standardized total effect
Change in 6MWT distance	−0.356		−0.356
Surgical duration	0.407		0.407
Serum albumin		−0.124	−0.124

motivation for rehabilitation. Therefore, large-scale multicenter studies are required to validate our findings. Second, the GIC patients did not all have the same type of surgery or surgical sites. Ideally, in a homogeneous group of GIC patients who underwent treatment, the target cancer for which preoperative physical rehabilitation is effective should be investigated. Third, the degree of compliance with the preoperative physical rehabilitation sessions was self-reported, and therefore, some bias is possible.

In conclusion, the improvement of gait ability using preoperative physical rehabilitation led to decreased PCs for GIC patients. Decreased PCs were also related to the surgical duration and baseline serum albumin.

ACKNOWLEDGMENTS

This study was funded by a Grant-in-Aid for Scientific Research (Grant no. 19K19880) from the Japan Society for the Promotion of Science. The authors thank the rehabilitation staff at the International University Health and Welfare Mita Hospital for their help with data collection.

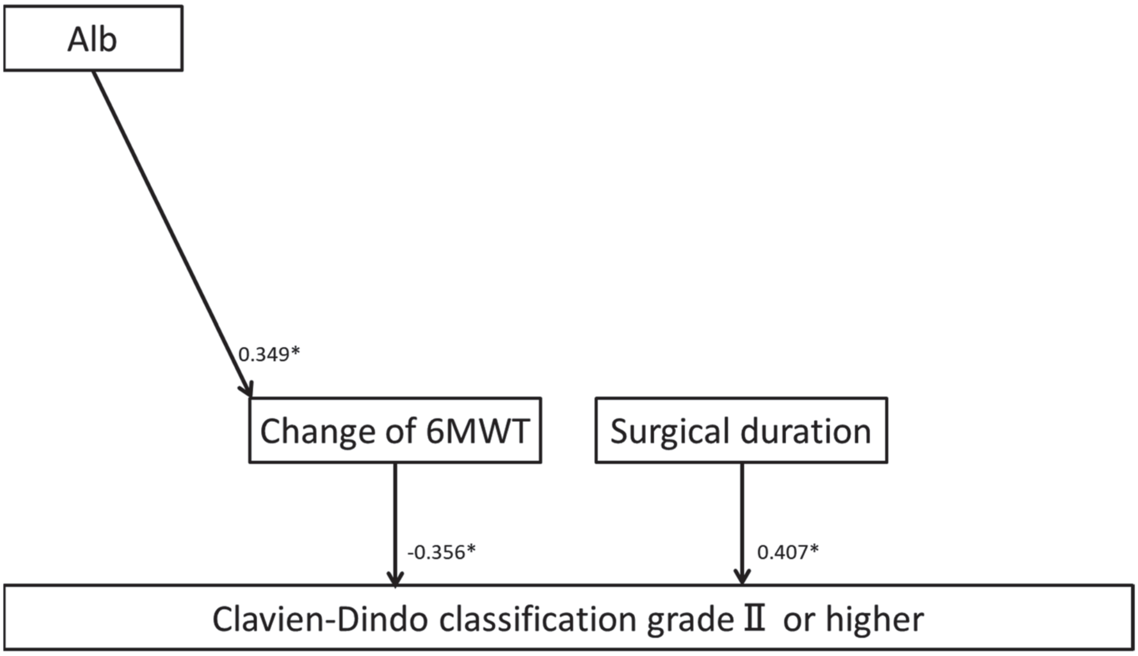

Fig. 3. Final model of factors leading to postoperative complications in patients with gastrointestinal cancer. For the variables shown in the figure, the path coefficients are standardized and the error variables are omitted. Parameters that were significantly correlated in the first model were included in the second model. Serum albumin (Alb) was found to be significantly and positively correlated with changes in the 6MWT distance, which was significantly and negatively correlated with postoperative complications. The surgical duration was significantly and positively correlated with postoperative complications. Model fit: χ^2=1.839, degrees of freedom=3, P=0.61, GFI=0.980, CFI=1.000, RMSEA=0.000, *P <0.05.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Brown SR, Mathew R, Keding A, Marshall HC, Brown JM, Jayne DG: The impact of postoperative complications on long-term quality of life after curative colorectal cancer surgery. Ann Surg 2014;259:916–923. DOI:10.1097/SLA.0000000000000407, PMID:24374539
2. Farid SG, Aldouri A, Morris-Stiff G, Khan AZ, Toogood GJ, Lodge JP, Prasad KR: Correlation between postoperative infective complications and long-term outcomes after hepatic resection for colorectal liver metastasis. Ann Surg 2010;251:91–100. DOI:10.1097/SLA.0b013e3181bfda3c, PMID:19858702
3. Chen CH, Ho-Chang, Huang YZ, Hung TT: Hand-grip strength is a simple and effective outcome predictor in esophageal cancer following esophagectomy with reconstruction: a prospective study. J Cardiothorac Surg 2011;6:98. DOI:10.1186/1749-8090-6-98, PMID:21843340
4. Smith TP, Kinasewitz GT, Tucker WY, Spillers WP, George RB: Exercise capacity as a predictor of post-thoracotomy morbidity. Am Rev Respir Dis 1984;129:730–734. DOI:10.1164/arrd.1984.129.5.730, PMID:6721272
5. Koch M, Antolovic D, Reissfelder C, Rahbari NN, Holoch J, Michalski I, Sweiti H, Ulrich A, Büchler MW, Weitz J: Leucocyte-depleted blood transfusion is an independent predictor of surgical morbidity in patients undergoing elective colon cancer surgery – a single-center analysis of 531 patients. Ann Surg Oncol 2011;18:1404–1411. DOI:10.1245/s10434-010-1453-x, PMID:21153884

6. Kubota T, Hiki N, Nunobe S, Kumagai K, Aikou S, Watanabe R, Sano T, Yamaguchi T: Significance of the inflammation-based Glasgow prognostic score for short- and long-term outcomes after curative resection of gastric cancer. J Gastrointest Surg 2012;16:2037–2044. DOI:10.1007/s11605-012-2036-x, PMID:23007284
7. Kvasnovsky CL, Adams K, Sideris M, Laycock J, Haji AK, Haq A, Nunoo-Mensah J, Papagrigoriadis S: Elderly patients have more infectious complications following laparoscopic colorectal cancer surgery. Colorectal Dis 2016;18:94–100. DOI:10.1111/codi.13109, PMID:26331365
8. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE: Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer 2012;107:931–936. DOI:10.1038/bjc.2012.350, PMID:22871883
9. Ozoya OO, Siegel EM, Srikumar T, Bloomer AM, DeRenzis A, Shibata D: Quantitative assessment of visceral obesity and postoperative colon cancer outcomes. J Gastrointest Surg 2017;21:534–542. DOI:10.1007/s11605-017-3362-9, PMID:28101721
10. Heger P, Probst P, Wiskemann J, Steindorf K, Diener MK, Mihaljevic AL: A systematic review and meta-analysis of physical exercise prehabilitation in major abdominal surgery (PROSPERO 2017 CRD42017080366). J Gastrointest Surg 2020;24:1375–1385. DOI:10.1007/s11605-019-04287-w, PMID:31228083
11. Hanaoka M, Yasuno M, Ishiguro M, Yamauchi S, Kikuchi A, Tokura M, Ishikawa T, Nakatani E, Uetake H: Morphologic change of the psoas muscle as a surrogate marker of sarcopenia and predictor of complications after colorectal cancer surgery. Int J Colorectal Dis 2017;32:847–856. DOI:10.1007/s00384-017-2773-0, PMID:28190101
12. Haruki K, Shiba H, Fujiwara Y, Furukawa K, Wakiyama S, Ogawa M, Ishida Y, Misawa T, Yanaga K: Negative impact of surgical site infection on long-term outcomes after hepatic resection for colorectal liver metastases. Anticancer Res 2013;33:1697–1703. PMID:23564818
13. Mörner M, Gunnarsson U, Jestin P, Egenvall M: Volume of blood loss during surgery for colon cancer is a risk determinant for future small bowel obstruction caused by recurrence—a population-based epidemiological study. Langenbecks Arch Surg 2015;400:599–607. DOI:10.1007/s00423-015-1317-8, PMID:26100567
14. Hu WH, Cajas-Monson LC, Eisenstein S, Parry L, Cosman B, Ramamoorthy S: Preoperative malnutrition assessments as predictors of postoperative mortality and morbidity in colorectal cancer: an analysis of ACS-NSQIP. Nutr J 2015;14:91. DOI:10.1186/s12937-015-0081-5, PMID:26345703
15. Inaoka K, Kanda M, Uda H, Tanaka Y, Tanaka C, Kobayashi D, Takami H, Iwata N, Hayashi M, Niwa Y, Yamada S, Fujii T, Sugimoto H, Murotani K, Fujiwara M, Kodera Y: Clinical utility of the platelet–lymphocyte ratio as a predictor of postoperative complications after radical gastrectomy for clinical T2-4 gastric cancer. World J Gastroenterol 2017;23:2519–2526. DOI:10.3748/wjg.v23.i14.2519, PMID:28465636
16. Mohri Y, Tanaka K, Toiyama Y, Ohi M, Yasuda H, Inoue Y, Kusunoki M: Impact of preoperative neutrophil to lymphocyte ratio and postoperative infectious complications on survival after curative gastrectomy for gastric cancer. Medicine (Baltimore) 2016;95:e3125. DOI:10.1097/MD.0000000000003125, PMID:26986164
17. Shiozaki A, Fujiwara H, Okamura H, Murayama Y, Komatsu S, Kuriu Y, Ikoma H, Nakanishi M, Ichikawa D, Okamoto K, Ochiai T, Kokuba Y, Otsuji E: Risk factors for postoperative respiratory complications following esophageal cancer resection. Oncol Lett 2012;3:907–912. DOI:10.3892/ol.2012.589, PMID:22741016
18. Tanaka Y, Kanda M, Tanaka C, Kobayashi D, Mizuno A, Iwata N, Hayashi M, Niwa Y, Takami H, Yamada S, Fujii T, Nakayama G, Sugimoto H, Fujiwara M, Kodera Y: Usefulness of preoperative estimated glomerular filtration rate to predict complications after curative gastrectomy in patients with clinical T2–4 gastric cancer. Gastric Cancer 2017;20:736–743. DOI:10.1007/s10120-016-0657-6, PMID:27734274
19. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M: The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–196. DOI:10.1097/SLA.0b013e3181b13ca2, PMID:19638912
20. Braga M, Ljungqvist O, Soeters P, Fearon K, Weimann A, Bozzetti F, ESPEN: ESPEN Guidelines on Parenteral Nutrition: Surgery. Clin Nutr 2009;28:378–386. DOI:10.1016/j.clnu.2009.04.002, PMID:19464088

21. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, Liberman AS, Stein B, Charlebois P, Feldman LS, Carli F: Prehabilitation *versus* rehabilitation. Anesthesiology 2014;121:937–947. DOI:10.1097/ALN.0000000000000393, PMID:25076007
22. Gillis C, Fenton TR, Sajobi TT, Minnella EM, Awasthi R, Loiselle SÈ, Liberman AS, Stein B, Charlebois P, Carli F: Trimodal prehabilitation for colorectal surgery attenuates post-surgical losses in lean body mass: a pooled analysis of randomized controlled trials. Clin Nutr 2019;38:1053–1060. DOI:10.1016/j.clnu.2018.06.982, PMID:30025745
23. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories: ATS Statement. Am J Respir Crit Care Med 2002;166:111–117. DOI:10.1164/ajrccm.166.1.at1102, PMID:12091180
24. Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R: Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85:115–122. DOI:10.1152/jappl.1998.85.1.115, PMID:9655763
25. Hooper D, Coughlan J, Mullen MR: Structural equation modelling: guidelines for determining model fit. Electron J Bus Res Methods 2008;6:53–60.
26. Sander LE, Sackett SD, Dierssen U, Beraza N, Linke RP, Müller M, Blander JM, Tacke F, Trautwein C: Hepatic acute-phase proteins control innate immune responses during infection by promoting myeloid-derived suppressor cell function. J Exp Med 2010;207:1453–1464. DOI:10.1084/jem.20091474, PMID:20530204
27. Allen JB, Allen FB: The minimum acceptable level of hemoglobin. Int Anesthesiol Clin 1982;20:1–22. DOI:10.1097/00004311-198202000-00003, PMID:6757141
28. Olsen GN: The evolving role of exercise testing prior to lung resection. Chest 1989;95:218–225. DOI:10.1378/chest.95.1.218, PMID:2642409
29. Ferguson MK, Lehman AG, Bolliger CT, Brunelli A: The role of diffusing capacity and exercise tests. Thorac Surg Clin 2008;18:9–17, v. DOI:10.1016/j.thorsurg.2007.11.001, PMID:18402197
30. Shoemaker WC, Appel PL, Kram HB: Tissue oxygen debt as a determinant of lethal and nonlethal postoperative organ failure. Crit Care Med 1988;16:1117–1120. DOI:10.1097/00003246-198811000-00007, PMID:3168504
31. Sheffield-Moore M, Yeckel CW, Volpi E, Wolf SE, Morio B, Chinkes DL, Paddon-Jones D, Wolfe RR: Postexercise protein metabolism in older and younger men following moderate-intensity aerobic exercise. Am J Physiol Endocrinol Metab 2004;287:E513–E522. DOI:10.1152/ajpendo.00334.2003, PMID:15149953