J. Phys. Ther. Sci. 32: 833–838, 2020

The Journal of Physical Therapy Science

Original Article

Does age of patients with gastrointestinal cancer impact postoperative physical function and quality of life? A prospective study using the new Japanese elderly standard

Tsuyoshi Hara, RPT, PhD[1)*], Eisuke Kogure, RPT, PhD[2)], Akira Kubo, RPT, PhD[1)]

[1)] *Department of Physical Therapy, School of Health Science, International University of Health and Welfare: 2600-1 Kitakanemaru, Ootawara-shi, Tochigi 324-8501, Japan*
[2)] *Rehabilitation Progress Center Inc, Japan*

Abstract. [Purpose] The purpose of this study was to investigate the relationship among aging factors using the new Japanese elderly standard, early postoperative physical function, and health-related quality of life (HRQOL) in patients with gastrointestinal cancer. [Participants and Methods] We studied 94 patients scheduled for elective surgery of gastrointestinal cancer: 53 males and 41 females aged 62.0 ± 12.1 years (mean ± SD). Patients were divided into three groups based on age at baseline: young (<65 years), pre-old (65–74 years), and old (≥75 years) groups. We measured body mass index, isometric knee extension force (IKEF), 6-minute walk test (6MWT), and Short-Form 36-Item Health Survey version 2 (SF-36) at baseline and 4 weeks after surgery. [Results] Patients 75 years or older had significantly lower IKEF and 6MWT compared to the other groups. Patients younger than 65 years had significantly greater scores on the mental health SF36 subscale 4 weeks after surgery compared to baseline. Comparatively, patients older than 75 years had significantly decreased mental health scores 4 weeks after surgery. [Conclusion] Based on the new Japanese elderly standard, advanced age appears to worsen the postoperative change of HRQOL in patients with gastrointestinal cancer.

Key words: Elderly, Gastrointestinal cancer, Postoperative quality of life

(This article was submitted Aug. 5, 2020, and was accepted Sep. 9, 2020)

INTRODUCTION

Previous work around the world has shown that aging of patients with gastrointestinal cancer increases perioperative risk factors, such as onset of postoperative complications[1, 2)], reduces postoperative health-related quality of life (HRQOL)[3)] and also reduced physical function after surgery[4)]. The International Society of Geriatric Oncology and National Comprehensive Cancer Network recommend the incorporation of geriatric assessment in treatment planning[5–7)]. Thus, the utility of geriatric assessment is being recognized increasingly in oncology.

The classification of "older" in Japan was previously defined as 65 years of age or higher, the same as other countries[8)]. Additionally, Japanese "older" was sub-classified two groups: the young-old, 65 to 74 years old, and the old-old, 75 years of age or older. However, medical advances and improved educational standards have prompted a revision of these standards. In particular, the physical function in older of 65 years of age of higher at 2006 were significantly increased compared with older at 1997. From these things, the Japan Geriatrics society proposed changing the definition of older to 75 years of age or older[8)]. Consequently, Japanese medical research needs to be reevaluated based on how this new Japanese elderly standard influences treatment progress of various diseases. As mentioned previously, important clinical outcome such as physical function and

*Corresponding author. Tsuyoshi Hara (E-mail: hara@iuhw.ac.jp)

HRQOL in patients with gastrointestinal cancer should be investigate how new Japanese elderly standard influences.

The purpose of this study was to investigate how this new Japanese elderly standard influences postoperative course such as physical function and HRQOL in surgical patients with gastrointestinal cancer at a single center.

PARTICIPANTS AND METHODS

This study was approved by the Research Ethics Board of the International University Health and Welfare Mita Hospital, Minato-ku, Tokyo, Japan. All study procedures were carried out in accordance with ethical standards (registration: 5-15-1). In addition, all participants received an explanation of the research and agreed to participate based on the Declaration of Helsinki. Participants were scheduled for elective surgery for gastrointestinal cancer or suspected gastrointestinal cancer at the International University Health and Welfare Mita Hospital between April 1, 2012, and December 31, 2017. Patients were excluded if the surgery was performed emergently, if the non-malignancy tumor was diagnosed after surgery, if it corresponded with a heavy impact postoperative course such as under the Dindo-Clavien classification[9] grade III or higher, or if the home discharge was difficult at the investigation period.

The following clinical data were collected prospectively: age at baseline, gender, clinical stage of cancer after surgery, comorbidities (hypertension, hyperlipidemia, diabetes mellitus, cardiac diseases, respiratory diseases, orthopedic diseases, and cerebrovascular diseases), diagnosis, received neoadjuvant therapy, type of surgical (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), C-reactive protein at 3 days after surgery, and length of hospital stay.

This was a prospective observational study at a single clinical center. Patients were evaluated for physical function and HRQOL at baseline (1–2 days prior to surgery) and 4 weeks after surgery. Perioperative care for all participants was managed by gastrointestinal surgeons based on the clinical course for resection of gastrointestinal cancer of International University Health and Welfare Mita Hospital. Study patients were divided into three age groups based on based on the new Japanese elderly standard[8]: the young group, under 65 years, the pre-old group, 65 to 74 years, and the old group, 75 years or older.

The following parameters were measured at baseline and 4 weeks after surgery: body mass index, isometric knee extension force (IKEF), exercise capacity, and HRQOL.

BMI was calculated by weight in kilograms measured while wearing clothes, and height in meters.

IKEF was evaluated using an isometric test device (HUR® 5530 leg extension/curl rehab machine, HUR Ltd, Kokkola, Finland). Patients performed a 5 second maximal effort of right knee extension twice in the sitting position on HUR manual. The evaluation value normalized the joint torque calculated from maximum value and distance from the knee joint space to the pad center by body mass.

Exercise capacity was evaluated using a 6-minute walk test (6MWT) based on the guidelines set forth by the American Thoracic Society[10]. Patients were instructed to walk back and forth along a 50-meter stretch of hallway for 6 minutes at pace representing maximal effort by the end of the walk. The total distance covered in 6 min was recorded in meters only once at each evaluation period.

HRQOL was evaluated using the 36-Item Short-Form Health Survey version 2 Acute, Japan (SF-36) based on previous studies[11, 12]. SF36 is a self-administered questionnaire which includes eight subscales: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Eight subscale scores were calculated using a scoring program as recommended by iHope International[13]. In this study, each subscale was scored from 0 to 100 points, with higher scores indicating higher HRQOL.

Clinical characteristics at baseline (i.e., age, surgical duration, blood loss and laboratory data) among the three groups (the young group, pre-old group and old group) were compared at baseline and post-surgery using the one-way analysis of variance for continuous variables. Categorical variables at baseline (i.e., gender, clinical stage of cancer, comorbidities and diagnosis) were compared using the χ^2 test.

The perioperative changes in the parameters such as BMI, IKEF, 6MWT, and SF-36 subscales among the three groups were analyzed with two-way analysis of variance for continuous variables. Additionally, parameters with significant interaction effects were compared using the simple main effect test. All statistical analyses were performed using SPSS version 24.0 (SPSS Inc, Chicago, IL, USA). A p-value of less than 0.05 was considered significant.

RESULTS

A total of 696 patients were approached for consent; of these, 399 declined consent (57%), 203 were excluded as per the exclusion criteria (29%), and 94 patients (14%) were included in the study (Fig. 1). Of the 94 patients 55 were assigned to the young group (8%), 25 to the pre-old group (4%), and 14 to the old group (2%) based on age at baseline. The baseline clinical characteristics of the three groups are shown in Table 1. The mean values of serum-albumin in the young group at baseline were significantly higher than the pre-old and old groups. The old group had a significantly higher ratio of patients on hypertension and open surgery compared to the young group.

Perioperative changes in BMI, IKEF, and 6MWT are shown in Table 2. The BMI was significantly decreased 4 weeks after surgery compared to baseline in all groups. However, IKEF and 6MWT was not different between baseline and 4 weeks

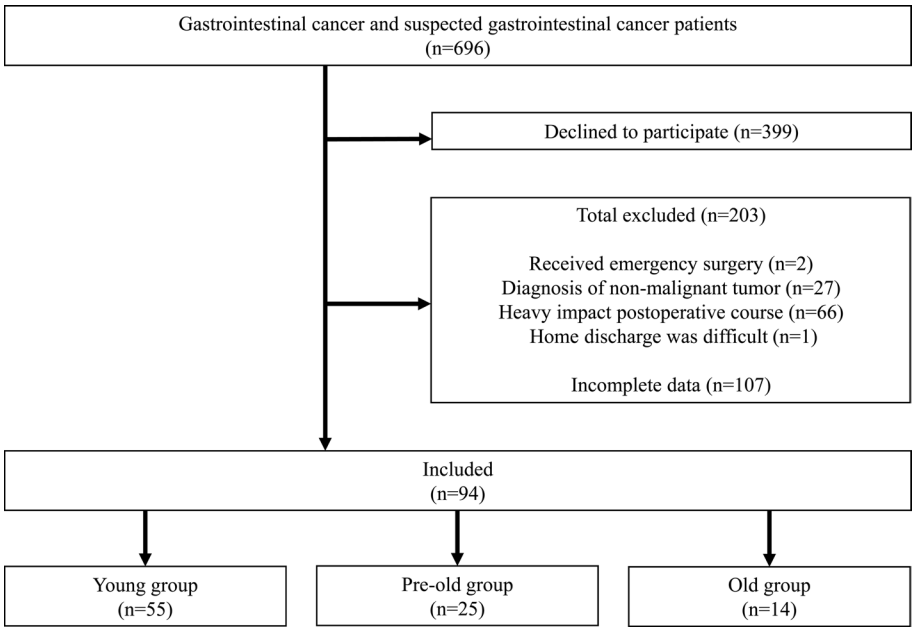

Fig. 1. Diagram for the study.

post-surgery. The mean values of IKEF and 6MWT in the old group were significantly decreased compared to the other two groups.

The perioperative changes in SF-36 subscales are shown in Table 2. Physical functioning, role physical, bodily pain, vitality, social functioning, and role emotional at 4 weeks after surgery were significantly decreased compared to baseline. There was no significant difference in general health and mental health between baseline and post-surgery. Physical functioning was significantly different among the three groups. The effect of surgery on mental health depended on age: the young group had significantly increased mental health from baseline to 4 weeks after surgery, but the old group had significantly decreased mental health (Table 2).

DISCUSSION

With regard to physical measures, only BMI was reduced after surgery in patients with gastrointestinal cancer (Table 2). This is consistent with previous studies, which showed that reduced BMI delayed improvements in physical function at after surgery in gastrointestinal patients[14]. In the HRQOL of patients with gastrointestinal cancer, SF-36 subscaled after surgery compared to before surgery; the general and mental health were significantly decreased (Table 2). A previous study of HRQOL pre-surgery and 6 weeks after discharge in patients with gastrointestinal cancer reported that only psychological function relating to depression was significantly decreased[3]. Our study is a relatively shorter follow up period than this previous work but is consistent with HRQOL pathognomonic changes early after surgery.

We observed exercise capacity and physical functioning reduced post-surgery (Table 2), with significant differences between the new Japanese elderly standard age groups. This is consistent with previous studies linking this to an age effect[3, 4, 11, 12]. This suggests that this new Japanese elderly standard captures the age-related reduction in exercise capacity in patients with gastrointestinal cancer. This is likely related to the reduction in muscle strength we observed in the older group (Table 2). This new Japanese elderly standard may also stratify differences in muscle weakness in elderly patients with gastrointestinal cancer. Additionally, the pre-old group, which corresponds to the formerly elderly group was not significantly different than the young group (Table 2). Thus, this may validate the new Japanese elderly standard of 75 years or older. In this study IKEF, which is a typical value of motor function in the elderly, could not be classified like 6MWT and HRQOL. Elderly patients with gastrointestinal cancer may be influenced by other factors such as additional comorbidities and type of surgery.

The young group significantly increased their mean value of mental health of SF-36 subscale from before to post-surgery, while the old group decreased mental health (Table 2). Based on these results, aging may affect the change in HRQOL in the early post-surgery period. The mental health SF-36 subscale is influenced by factors such as spiritual fatigue and stress[13]. Previous studies stress that mental health, such as depression and fatigue, should be prevented and treated in elderly cancer patients[15, 16]. In addition, cancer-related chronic fatigue is present in 70%–100% of cancer patients, especially during active treatment[17]. The biological mechanisms are currently unclear, although several proposed mechanisms include serotonin

Table 1. Clinical characteristics

		Young group n=55	Pre-old group n=25	Old group n=14
Age (years)		54.1 ± 8.6	69.4 ± 2.6*	79.9 ± 3.6* **
Gender	Female	24 (44)	10 (40)	7 (50)
	Male	31 (56)	15 (60)	7 (50)
Clinical stage of the cancer	I	19 (35)	9 (36)	4 (29)
	II	11 (20)	7 (28)	2 (14)
	III	20 (36)	7 (28)	5 (36)
	IV	5 (9)	2 (8)	3 (21)
Comorbidities	Hypertension	7 (13)	9 (36)	7 (50†)
	Hyperlipidemia	3 (5)	1 (4)	1 (7)
	Diabetes mellitus	4 (7)	4 (16)	1 (7)
	Cardiac diseases	2 (4)	2 (8)	1 (7)
	Respiratory diseases	3 (5)	2 (8)	1 (7)
	Orthopedic diseases	2 (4)	1 (4)	1 (7)
	Cerebrovascular diseases	0 (0)	2 (8)	2 (14)
Diagnosis	Esophagus cancer	2 (4)	1 (4)	1 (7)
	Gastric cancer	1 (2)	4 (16)	0 (0)
	Liver cancer	3 (5)	1 (4)	3 (21)
	Gallbladder cancer	0 (0)	2 (8)	0 (0)
	Bile duct cancer	0 (0)	0 (0)	1 (7)
	Pancreatic cancer	5 (9)	4 (16)	1 (7)
	Colon cancer	23 (42)	8 (32)	5 (36)
	Rectal cancer	21 (38)	5 (20)	3 (21)
Received neoadjuvant therapy		5 (9)	1 (4)	0 (0)
Type of surgery	Open surgery	9 (16)	10 (40)	7 (50†)
	Laparoscopic surgery	46 (84)	15 (60)	7 (50)
Surgery duration (min)		275.4 ± 104.9	287.4 ± 95.2	247.8 ± 101.4
Blood loss (mL)		275.9 ± 626.0	243.4 ± 359.8	268.1 ± 419.8
Blood transfusion (mL)	Red cell concentrates	157.8 ± 637.0	134.4 ± 334.4	80.0 ± 299.3
	Fresh frozen plasma	50.2 ± 273.0	28.8 ± 144.0	68.6 ± 256.6
Laboratory data	Serum-albumin (mg/dL)	4.5 ± 0.3	4.2 ± 0.5*	4.2 ± 0.4*
	C-reactive protein (mg/dL)	0.20 ± 0.38	1.00 ± 3.14	0.18 ± 0.21
	C-reactive protein at 3 days after surgery (mg/dL)	8.83 ± 6.23	11.65 ± 6.46	12.31 ± 8.37
Length of hospital stay (days)		16.5 ± 8.2	21.3 ± 12.5	21.2 ± 8.9

Values are numbers (%) or mean ± standard deviation.
*Significant difference from young group (Bonferroni), **Significant difference from pre-old group (Bonferroni).
†Significant difference from young group (χ^2 test).

dysregulation, endocrine dysfunction, circadian rhythm disruption, and cytokine dysregulation; multiple mechanisms may be at play[15–17]. Elderly patients with gastrointestinal cancer as classified by new Japanese elderly standard may need to address the decrements in HRQOL at after surgery, perhaps with comprehensive intervention such as adjustments circadian rhythm in hospital and counseling by clinical psychologists.

In conclusion, based on the new Japanese elderly standard, elderly patients with gastrointestinal cancer appear to have reduced physical and HRQOL before and after surgery, and also early postoperative changes in HRQOL.

There are some limitations of this study. First, the generalizability of the results of this study is limited due to the relatively small number of patients with gastrointestinal cancer at a single institute. Future studies should repeat this study with a larger number of patients from multiple institutions. Second, some other factors which were different between the young and old group were not examined in this study. Ideally, the relationship between elderly patients with gastrointestinal cancer and hypertension comorbidity or receiving open surgery should re-investigated in detail. Finally, physical activity from discharge to 4 weeks after surgery were not reported, and thus might be confounders to the follow up measures. Future studies should monitor and consider the physical activity at discharge.

Table 2. Perioperative changes of each parameter at baseline to 4 weeks after surgery

			Baseline	4 weeks after surgery
Body mass index		Young group	23.3 ± 5.0	22.3 ± 4.4*
		Pre-old group	23.6 ± 3.4	22.2 ± 3.6
		Old group	22.8 ± 2.5	22.0 ± 2.6
Isometric knee extension force		Young group	4.87 ± 1.59	4.82 ± 1.48
		Pre-old group	4.36 ± 1.64	4.12 ± 1.26
		Old group ** †	3.01 ± 1.06	3.03 ± 0.94
6-minute walk test		Young group	556.0 ± 76.8	556.3 ± 94.1
		Pre-old group **	509.1 ± 68.2	498.3 ± 74.9
		Old group ** †	442.7 ± 86.2	416.4 ± 83.7
SF-36 subscales	Physical functioning	Young group	91.6 ± 9.1	84.6 ± 13.2*
		Pre-old group **	84.8 ± 14.5	76.2 ± 18.4
		Old group ** †	74.3 ± 21.1	64.3 ± 21.0
	Role physical	Young group	85.8 ± 24.2	63.7 ± 27.7*
		Pre-old group	79.0 ± 19.3	55.0 ± 29.1
		Old group	67.4 ± 29.9	58.9 ± 25.1
	Bodily pain	Young group	83.4 ± 18.8	65.3 ± 22.1*
		Pre-old group	77.3 ± 19.8	65.9 ± 19.7
		Old group	69.7 ± 33.2	68.9 ± 26.1
	General health	Young group	60.4 ± 14.4	62.6 ± 14.1
		Pre-old group	55.1 ± 14.3	56.6 ± 16.0
		Old group	56.5 ± 16.4	53.6 ± 16.1
	Vitality	Young group	66.3 ± 15.6	63.9 ± 15.3*
		Pre-old group	63.3 ± 17.4	58.5 ± 17.3
		Old group	67.9 ± 20.9	55.4 ± 21.8
	Social functioning	Young group	79.8 ± 20.9	69.5 ± 26.8
		Pre-old group	76.5 ± 24.0	63.0 ± 31.6
		Old group	77.7 ± 24.1	65.2 ± 31.5
	Role emotional	Young group	86.3 ± 18.3	74.7 ± 26.6*
		Pre-old group	74.7 ± 22.2	62.7 ± 29.1
		Old group	72.0 ± 33.1	70.8 ± 32.8
	Mental health ‡	Young group	69.7 ± 17.8	75.9 ± 13.7[1)]
		Pre-old group	66.6 ± 23.4	71.0 ± 18.3
		Old group	71.4 ± 23.7	62.9 ± 22.2[2)]

Values are mean ± standard deviation. SF-36: Short-Form 36-Item Health Survey; ANOVA: analysis of variance.
*Significant difference from baseline (two-way analysis of variance), **Significant difference from young group (Bonferroni), †Significant difference from pre-old group (Bonferroni), ‡Significant interaction effect (two-way analysis of variance).
[1)] Significant increase for simple main effect test (Bonferroni) when compared with the young group at baseline.
[2)] Significant decrease for simple main effect test (Bonferroni) when compared with the young group at 4 weeks after surgery.

Funding

This study was funded by The Grants-in-Aid for Scientific Research (grant number: 19K19880) from the Japan Society for the Promotion of Science.

Conflict of interest

None.

ACKNOWLEDGMENT

We thank the rehabilitation staff at the International University Health and Welfare Mita Hospital for their help with the data collection.

REFERENCES

1) Koch M, Antolovic D, Reissfelder C, et al.: 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. [Medline] [CrossRef]
2) Kvasnovsky CL, Adams K, Sideris M, et al.: Elderly patients have more infectious complications following laparoscopic colorectal cancer surgery. Colorectal Dis, 2016, 18: 94–100. [Medline] [CrossRef]
3) Sharma A, Sharp DM, Walker LG, et al.: Predictors of early postoperative quality of life after elective resection for colorectal cancer. Ann Surg Oncol, 2007, 14: 3435–3442. [Medline] [CrossRef]
4) Kogure E, Hara T, Ishii T, et al.: Changes in fatigue and physical function with age for patients with gastrointestinal cancer in the perioperative period: a comparison between older and young patients. J Phys Ther Sci, 2017, 29: 2004–2008. [Medline] [CrossRef]
5) Decoster L, Van Puyvelde K, Mohile S, et al.: Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. Ann Oncol, 2015, 26: 288–300. [Medline] [CrossRef]
6) Pallis AG, Fortpied C, Wedding U, et al.: EORTC elderly task force position paper: approach to the older cancer patient. Eur J Cancer, 2010, 46: 1502–1513. [Medline] [CrossRef]
7) VanderWalde N, Jagsi R, Dotan E, et al.: NCCN guidelines insights: older adult oncology, version 2.2016. J Natl Compr Canc Netw, 2016, 14: 1357–1370. [Medline] [CrossRef]
8) Arai H: [Definition of older people: time to reconsider the definition?]. Nippon Ronen Igakkai Zasshi, 2019, 56: 1–5. [Medline] [CrossRef]
9) Clavien PA, Barkun J, de Oliveira ML, et al.: The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg, 2009, 250: 187–196. [Medline] [CrossRef]
10) ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories: ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med, 2002, 166: 111–117. [Medline] [CrossRef]
11) Lundy JJ, Coons SJ, Wendel C, et al.: Exploring household income as a predictor of psychological well-being among long-term colorectal cancer survivors. Qual Life Res, 2009, 18: 157–161. [Medline] [CrossRef]
12) Trentham-Dietz A, Remington PL, Moinpour CM, et al.: Health-related quality of life in female long-term colorectal cancer survivors. Oncologist, 2003, 8: 342–349. [Medline] [CrossRef]
13) Fukuhara S, Suzukamo Y: Manual of SF-36v2 Japanese version. Kyoto: iHope International, 2019.
14) Hara T, Kubo A: The perioperative changes in physical function and physique of patients with gastrointestinal cancer. J Phys Ther Sci, 2015, 27: 693–695. [Medline] [CrossRef]
15) Naeim A, Aapro M, Subbarao R, et al.: Supportive care considerations for older adults with cancer. J Clin Oncol, 2014, 32: 2627–2634. [Medline] [CrossRef]
16) Rao A, Cohen HJ: Symptom management in the elderly cancer patient: fatigue, pain, and depression. J Natl Cancer Inst Monogr, 2004, 32: 150–157. [Medline] [CrossRef]
17) Gerber LH, Stout N, McGarvey C, et al.: Factors predicting clinically significant fatigue in women following treatment for primary breast cancer. Support Care Cancer, 2011, 19: 1581–1591. [Medline] [CrossRef]