Preoperative physical activity predicts postoperative functional recovery in gastrointestinal cancer patients

（消化器がん患者において術前身体活動量は術後身体機能回復を予測する）

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リハビリテーション療法学専攻

理学療法学分野

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1. Abstract

【Introduction】

Postoperative functional decline in patients with gastrointestinal cancer may affect subsequent adjuvant treatment (e.g., chemotherapy). In order to take early action against these problems, it is important to predict postoperative functional decline. It has been reported that low physical activity (PA) and prolonged sedentary time in the elderly are associated with functional decline, suggesting that people with low PA or prolonged sedentary time have a higher risk of functional decline in the future. In patients with gastrointestinal cancer, it has been reported that preoperative PA is associated with the ability to stand without assistance after surgery and postoperative hospital stay, suggesting that preoperative PA influences postoperative functional recovery. However, the ability to stand up without assistance after surgery is an index that mainly reflects lower limb muscle strength, and postoperative hospital stay is reported to be affected by social factors, so it is difficult to say that these are index that reflects postoperative functional recovery. On the other hand, 6-minute walking distance (6MWD) has been reported to be a valid indicator of postoperative functional recovery in patients with gastrointestinal diseases. However, there are no studies to investigate the relationship between preoperative PA or sedentary time and postoperative functional recovery objectively assessed by 6MWD in patients with gastrointestinal cancer.

【Purpose】

The present study aimed to investigate the association between preoperative PA or sedentary time and postoperative functional recovery in gastrointestinal cancer patients.

【Methods】

In this prospective study, we included 101 patients who underwent colorectal or gastric cancer surgery. Primary outcome was 6MWD decline ratio [(postoperative 6MWD value – preoperative 6MWD value) / preoperative 6MWD value × 100 (%)], which was determined as postoperative functional recovery. Patients were divided into two groups according to the median of 6MWD decline ratio: above the median (non-decline group) and below the median (decline group). The International Physical Activity Questionnaire (IPAQ-SV) (the usual seven-day short version) was used to assess preoperative PA and sedentary time. Multivariate logistic regression analysis was performed to identify predictive factors of postoperative functional recovery.

【Results】

The median of 6MWD decline ratio was -9.0 %. Preoperative PA [odds ratio (OR): 3.812; 95% confidence interval (CI): 1.326–10.956; p= 0.01], 6MWD (OR: 1.006; 95% CI: 1.002–1.011; p<0.01), C-reactive protein (OR: 4.138; 95% CI: 1.383–12.377; p=0.01), and combined resection (OR: 3.425; 95% CI: 1.101–10.649; p=0.03) were associated with postoperative functional recovery.

【Conclusion】

Preoperative PA is a predictor of postoperative functional recovery in patients who undergoing gastrointestinal cancer surgery.

1. 要旨

【背景】

消化器がん患者の術後身体機能低下は、その後の補助治療（化学療法など)に影響を及ぼすことが考えられる。これらに対して早期から対策を行うためには、術後身体機能低下を予測することが重要である。高齢者における低身体活動と座位時間の長期化は身体機能低下と関連することが報告されており、低身体活動または座位時間の長期化は将来的な身体機能低下と関連することが示唆される。消化器がん患者においても、術前の身体活動量は術後の介助なしでの起立の可否や術後在院日数と関連することが報告されており、術前の身体活動量は術後身体機能回復に影響を及ぼすことが推測される。しかしながら、術後の介助無しでの起立の可否は主に下肢筋力を反映した指標であること、術後在院日数は社会的要因の影響を受けることが報告されているため、これらは術後の全身的な身体機能回復を十分に反映した指標とは言い難い。一方で消化器疾患患者において、6 分間歩行距離(6-minute walk distance: 6MWD)は術後回復の指標として妥当性があることが報告されているが、消化器がん患者において術前の身体活動量または座位時間と 6MWD を用いて客観的に評価した術後身体機能回復との関連を調査した研究は見当たらない。

【目的】

本研究の目的は、消化器がん患者において術前身体活動量または座位時間と術後身体機能回復との関連を明らかにすることとした。

【方法】

本研究は前向き観察研究であり、101 例の大腸がんまたは胃がん患者を解析対象とした。アウトカムは術後身体機能回復の指標として 6MWD 低下率［(術後 6MWD 値 − 術前 6MWD 値) / 術前 6MWD 値 × 100 (%)]とした。対象者は 6MWD 低下率の中央値を基準に、中央値以上（非低下群)と中央値未満（低下群)に群分けした。術前身体活動量と座位時間は International Physical Activity Questionnaire Short Version usual week (IPAQ-SV)を用いて評価した。術後身体機能回復の予測因子を明らかにするために、ロジスティック回帰分析を実施した。

【結果】

6MWD 低下率の中央値は-9.0%であった。術前身体活動量［odds ratio (OR): 3.812; 95% confidence interval (CI): 1.326–10.956; p=0.01]、6MWD (OR: 1.006; 95% CI: 1.002–1.011; p<0.01)、C 反応性蛋白（OR: 4.138; 95% CI: 1.383–12.377; operative functional recovery. p=0.01)、他臓器合併切除（OR: 3.425; 95% CI: 1.101–10.649; p=0.03)はそれぞれ独立して術後身体機能回復と関連した。

【結論】

手術を受ける消化器がん患者において、術前身体活動量は術後身体機能回復の予測因子となる可能性が示唆された。

2. Introduction

Globally, gastrointestinal cancers, such as colorectal and gastric cancers, are some of the most frequently diagnosed cancers in both sexes [1]. Patients who undergo abdominal surgery experience postoperative functional decline, and cancer has been reported as a risk factor for postoperative prolonged functional decline [2]. Furthermore, the percentage of patients who did not return to their preoperative level of physical function 6 months after surgery was approximately 30% among patients who underwent abdominal surgery [2]. Physical function and performance status are negatively correlated in patients with cancer [3], and performance status before chemotherapy, including adjuvant chemotherapy, has been associated with chemotherapy toxicities in patients with gastrointestinal cancer [4]. As postoperative functional decline may negatively impact the subsequent treatment, it is important to predict, prevent, and reduce postoperative functional decline.

Physical activity (PA) is one of the modifiable factors associated with physical function [5]. We have reported that sedentary time, one of the PA indexes, was associated with postoperative complications [6] and PA has been reported to be associated with postoperative complications [7]. Thus, PA index are important factors affecting the postoperative course in patients with gastrointestinal cancer. Previous longitudinal studies have reported that low PA and longer sedentary time adjusted PA were associated with functional decline in older people and suggested that people with low PA or longer sedentary time have a higher risk of functional decline in the future [8,9]. In

gastrointestinal cancer patients, it has been reported that preoperative PA was related to postoperative recovery, such as an ability to stand unassisted after surgery, and postoperative hospital stay [10,11]. Although it is speculated that preoperative PA may affect postoperative recovery in patients with gastrointestinal cancer, an ability to stand unassisted mainly reflects lower limb muscle strength, and prolonged postoperative hospital stay is reportedly influenced by social factors [12]. Therefore, an ability to stand unassisted and postoperative hospital stay is not an adequate indicator of postoperative functional recovery. Hence, the association between preoperative PA or sedentary time and postoperative functional recovery assessed by outcomes that are more strongly reflect functional recovery needs to be clarified.

The 6-minute walk distance (6MWD) is a useful assessment of physical function and is widely used in the field of rehabilitation. 6MWD is also reportedly a valid indicator of postoperative recovery in patients undergoing gastrointestinal surgery [13,14]. A previous study reported that the mean 6MWD in patients undergoing gastrointestinal surgery reduced from 478 m preoperatively to 429 m at 3 weeks postoperatively [13], and that this decrease was greater than the minimal clinically important difference of 14 m for 6MWD in patients undergoing colorectal surgery [15], indicating that a large postoperative functional decline may also occur in patients undergoing gastrointestinal cancer surgery. However, the association between preoperative PA or sedentary time and

postoperative functional recovery measured by 6MWD has not been clear in patients with gastrointestinal cancer.

3. Purpose

The purpose of this study was to investigate the association between preoperative PA or sedentary time and postoperative functional recovery measured by 6MWD in patients with gastrointestinal cancer.

4. Materials and Methods

4.1 Study design, patients, and ethics

In this prospective study, 101 patients who underwent open or laparoscopic surgery for primary colorectal (n=76) or gastric cancer (n=25) between October 2016 and August 2020 at Kamiiida Daiichi General Hospital were enrolled. Exclusion criteria were patients who (1) needed assistance to walk preoperatively, (2) had cognitive dysfunction preoperatively, (3) had simultaneous cancer, (4) underwent palliative surgery, (5) had postoperative hospital stay of >3 weeks, and (6) missing data. All patients underwent rehabilitation from the day after surgery (twice a day on week-days and once on Saturdays), including mobilization; ambulation; and breathing, aerobic, and muscle strength exercises. This study was approved by the ethics committee of Kamiiida Daiichi

General Hospital and Nagoya University School of Medicine. Prior to participation, all patients were provided with a thorough explanation of the study and provided written consent in accordance with the Declaration of Helsinki.

4.2 Outcome

The primary outcome was 6MWD decline ratio [(postoperative 6MWD value - preoperative 6MWD value)/preoperative 6MWD ×100 (%)] calculated according to a previous study [16], which was determined as postoperative functional recovery. The 6MWD was measured within 1 week before surgery (preoperative 6MWD) and 1–3 days before discharge (postoperative 6MWD) according to a standardized procedure described by the American Thoracic Society Committee on proficiency standards for clinical pulmonary function laboratories [17]. Patients were instructed to walk the predetermined course as far as possible for 6 min.

4.3 Preoperative physical activity and sedentary time

Preoperative PA and sedentary time were assessed using the Japanese version of the usual seven-day short version of the International Physical Activity Questionnaire (IPAQ-SV) within 1 week before surgery. This questionnaire was used to assess vigorous- to moderate-intensity PA and walking activity during the usual seven days and sedentary time during the usual a weekday [18,19]. Each activity type and intensity score were assigned a metabolic equivalent (MET) value according

to the published protocol (e.g., METs for vigorous intensity = 8.0, moderate intensity = 4.0, walking = 3.3) [20]. Patients were classified into three groups (e.g., high, moderate, and low) according to the published IPAQ scoring protocol. We then defined high and moderate as "active", and low as "inactive" according to a previous study [21].

4.4 Preoperative muscle strength and gait speed

Grip strength was measured once on each side using a dynamometer (Grip-D, TKK 5401; Takei Scientific Instruments Co., Niigata, Japan), and the average of each pair of measurements was calculated [22]. Usual gait speed was measured over a 10-m distance between the 3- and 13-m marks of a 16-m walkway [23]. These measurements were obtained within 1 week before surgery.

4.5 Patient characteristics, surgery-related variables, and data collection

Age, gender, body mass index, Brinkman index, presence of polypharmacy, pulmonary function, presence of comorbidities, eastern cooperative oncology group performance status, cancer type (colorectal or gastric), and pathological TNM stage were recorded as patient characteristics. Polypharmacy was defined as intake of five or more daily medications [24].

Surgery-related variables including surgical approach (open or laparoscopic), combined resection, operative time, blood loss, and postoperative complications and postoperative hospital

stay were recorded. CD classification was used to grade postoperative complications (grades 1–5) [25,26]. To eliminate the possibility of description bias in patient records, grade 1 complications were excluded, and complications above CD grade 2 were considered postoperative complications.

The preoperative serum levels of albumin, C-reactive protein (CRP), and hemoglobin, and white blood cell and total lymphocyte counts were collected from electronic medical records. The prognostic nutrition index (PNI), a nutritional status indicator, was assessed using the following equation: PNI = 10 × serum albumin (mg/dL) + 0.005 × total lymphocyte count [27].

4.6 Statistical analysis

All continuous variables were expressed as medians (interquartile ranges). Patients were divided into the following two groups according to the median of 6MWD decline ratio: above the median (non-decline group) and below the median (decline group). Differences between the two groups were analyzed using the chi-squared test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Multivariate logistic regression analysis was performed to identify predictive factors for postoperative functional recovery. Variables with $p<0.10$ in univariate analysis were entered as independent variables in multivariate analysis. Multivariate logistic regression analysis was performed with (model 2) and without (model 1) sedentary time

adjustment. All statistical analyses were performed using EZR version 1.40 (Saitama Medical Center, Jichi Medical University, Shimotsuke, Japan) [28].

5. Results

The median of 6MWD decline ratio was –9.0 % (figure 1). After dividing patients into two groups based on the median of 6MWD decline ratio, 51 patients were assigned to the non-decline group and 50 patients to the decline group. There was no significant decrease in 6MWD in the non-decline group [preoperative vs. postoperative: 460 (370–510) vs. 455 (390–510); p=0.39], although there was a significant decrease in 6MWD in the decline group [preoperative vs. postoperative: 505 (431–572) vs. 397 (308–462); p<0.01] during the study period [median postoperative hospital stay: 12 (10−14) days] (figure 2). On analyses of patient characteristics, and comparisons of characteristics and measured variables between the two groups (table 1), no significant differences were observed, except for preoperative PA, 6MWD, CRP, and combined resection. Patients who were inactive tended to be more, and with combined resection were significantly more in the decline group than in the non-decline group (p=0.07 and p=0.04, respectively). Preoperative 6MWD and CRP levels were significantly higher in the decline group than in the non-decline group (p=0.01 and p=0.02, respectively).

Preoperative PA, 6MWD, CRP, and combined resection had a value of $p<0.10$ on univariate analysis, and underwent multivariate analysis as potential factors for postoperative functional recovery (table 2). Preoperative PA [odds ratio (OR): 3.812; 95% confidence interval (CI): 1.326–10.956; p=0.01], 6MWD (OR: 1.006; 95% CI: 1.002–1.011; $p<0.01$), CRP (OR: 4.138; 95% CI: 1.383–12.377; p=0.01), and combined resection (OR: 3.425; 95% CI: 1.101–10.649; p=0.03) were identified as predictive factors for postoperative functional recovery, independently of preoperative sedentary time. The OR for the occurrence of postoperative functional decline was shown in increments of 1 m in 6MWD and 1.00 mg/dL in CRP level.

6. Discussion

The main finding of the present study was that preoperative PA was positively associated with postoperative functional recovery, independent of sedentary time in patients who underwent gastrointestinal cancer surgery. Our study was the first to investigate the association between preoperative PA and postoperative functional recovery by measuring 6MWD in patients who underwent gastrointestinal cancer surgery. Previous studies have reported that regular preoperative exercise habits were related to postoperative early ambulation in patients who underwent open abdominal aortic aneurysm surgery [29] and preoperative step counts were correlated with postoperative step counts in colorectal cancer patients [30]. In a previous randomized control trial

comparing the early mobilization group with the normal group of patients who underwent abdominal cancer surgery, postoperative 6MWD was significantly higher in the early mobilization group than in the normal group [31]. It was speculated that preoperative inactive patients might take longer to progress to postoperative mobilization and might delay postoperative improvement in physical function. Furthermore, Yasunaga et al. reported that the time spent in moderate-to-vigorous intensity PA was more strongly associated with physical function than sedentary time among community-dwelling older people [32]. Thus, moderate-to-vigorous intensity PA might be a strong factor influencing short-term postoperative functional recovery compared to sedentary time.

Independent of PA, preoperative 6MWD was found to be associated with postoperative functional recovery in our study. Tahiri et al. reported that patients with higher preoperative physical function were more likely to experience postoperative functional decline after abdominal surgery [2]. Another previous study also indicated that patients with lower preoperative 6MWD had greater improvement in 6MWD with prehabilitation compared to patients with higher preoperative 6MWD in colorectal cancer patients [33]. The results of the present study support the results of these previous studies and it was suggested that postoperative rehabilitation might have resulted in better improvement in 6MWD in patients with lower preoperative 6MWD. Therefore, it was assumed that preoperative PA and physical function might respectively affect postoperative functional recovery.

In the present study, preoperative CRP level was related to postoperative functional recovery assessed by 6MWD. A previous study showed that postoperative CRP was associated with preoperative CRP in colorectal cancer patients [34]. It has also been reported that CRP is associated with skeletal muscle mass loss [35], and skeletal muscle mass was associated with cardiorespiratory fitness in community-dwelling people [36]. The 6MWD was associated with peak oxygen consumption in patients with gastrointestinal disease [37]. It was suggested that patients with higher preoperative CRP might also have postoperative hyperinflammation and reduced skeletal muscle mass, which might lead to postoperative functional decline evaluated by 6MWD.

We reported that the presence of combined resection was associated with postoperative functional decline. Previous studies indicated that operative time was significantly longer in patients with than without combined resection in cases of colorectal and gastric cancers, wherein patients underwent laparoscopic surgery [38, 39]. In addition, the longer the operative time, the poorer the recovery of physical function according to the questionnaire recorded after 1 month postoperatively in colorectal cancer patients [40]. In our study, operative time was significantly longer in patients with than without combined resection [303 (257–381) vs. 246 (186–318); $p<0.01$]. Therefore, it was presumed that the risk of postoperative functional decline increased because physical burden increased due to prolonged operative time by combined resection.

In recent years, prehabilitation, which involves preoperative exercise interventions to improve postoperative outcomes, has received much attention. A previous study reported that prehabilitation improved preoperative and postoperative 6MWD in colorectal cancer patients [41]. To prevent postoperative functional decline, we need to focus not only on improving preoperative functional capacity, but also on increasing PA. Previous studies indicated that resistance training reduced CRP in community-dwelling older people with high CRP > 1.0 mg/ dL [42], and exercise intervention reduced CRP in cancer survivors [43]. It has been suggested that inflammatory suppression through exercise intervention may be one of the key factors in preventing postoperative functional decline in perioperative gastrointestinal cancer patients.

The present study indicated that the median preoperative 6MWD and 6MWD decline ratio were 470 m and –9.0%, respectively. A previous study has reported that 6MWD reduced, on an average, from 478 m preoperatively to 429 m at 3 weeks postoperatively in patients with gastrointestinal surgery [13]. Although the number of days between surgery and postoperative 6MWD measurement was lower in the present study than in the previous study, the degree of 6MWD decline was similar in both studies [13]. Therefore, postoperative functional recovery may be better in the present study than that in the previous study. Previous studies have also reported that the postoperative rehabilitation and age can affect postoperative physical function [44, 2]. Therefore, the amount of postoperative rehabilitation in the present study may be more than that in the previous

study (the presence or absence of postoperative rehabilitation in the previous study is unclear), and the inclusion of younger patients (< 65-years-old) were also included may have influenced the results of the present study.

Our study has several limitations. First, patients with PS ≥ 2 were excluded from this study, which means that high-risk patients were excluded, resulting in a possible selection bias. Second, present study's results cannot be applied to patients who developed severe postoperative complications because patients who had a postoperative hospital stay of longer than 3 weeks were excluded to reduce the influence of social factors and, consequently, patients who developed severe postoperative complications were also excluded. Third, although postoperative hospital stay was not associated with the 6MWD decline ratio in this study ($r=0.17$; $p=0.07$), the effect of postoperative hospital stay on postoperative functional recovery cannot be completely ruled out. Therefore, future studies with a unified measurement date are necessary. Fourth, the results may not adequately adjust for confounding factors owing to the small sample size. Thus, our results must be interpreted with caution. Fifth, the present study included patients who underwent colorectal and gastric surgeries. Further studies are necessary to separately analyze patients with colorectal and gastric cancers. Sixth, data on the postoperative course, such as postoperative ambulation process and course of inflammation values, have not been measured. Further study is needed to investigate association between preoperative PA and postoperative ambulation process in patients with gastrointestinal

cancer. Finally, due to a limitation of the 6MWD measurement, our study found a couple of patients with a 6MWD decline ratio of plus 65%. Therefore, the actual functional decline in 6MWD might have been a little large.

7. Conclusion

The present study demonstrated that preoperative PA could predict postoperative functional recovery in patients who underwent gastrointestinal cancer surgery.

8. Acknowledgements

We thank all patients who participated in the present study, collaborating surgeons, and other medical staff for their important contributions to our study. This work was supported in part by JSPS KAKENHI (Grant Number 18H03127 to H. Sugiura) from the Japan Society for the Promotion Science. We would like to thank Editage (www.editage.com) for English language editing.

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the Department of General Health Sciences, Nagoya University Graduate School of Medicine, for their guidance and advice in writing my doctoral thesis.

Table 1. Characteristics of overall patients and comparison of characteristics and measured variables between two groups.

	overall (n=101)	non-decline group (n=51)	decline group (n=50)	p value
Age, years	69 (63–77)	70 (59–77)	68 (63–76)	0.62
Gender, n (male/female)	62 / 39	29 / 22	33 / 17	0.34
BMI, kg/m^2	22.5 (19.8–25.1)	22.3 (19.8–25.0)	22.7 (19.7–25.4)	0.67
Brinkman index	400 (0–690)	300 (0–600)	400 (0–727.5)	0.34
Polypharmacy, n (yes/no)	40 / 61	24 / 27	16 / 34	0.12
%VC, %	96.4 (87.1–107.6)	100.0 (86.8–107.8)	94.8 (87.3–107.4)	0.67
FEV1.0%, %	78.3 (73.5–82.7)	79.8 (75.4–83.7)	77.1 (70.2–82.3)	0.10
PS, n (0/1)	86 / 15	46 / 5	40 / 10	0.15
Comorbidities				
DM, n (yes/no)	27 / 74	14 / 37	13 / 37	0.86
CVD, n (yes/no)	9 / 92	4 / 47	5 / 45	0.74
COPD, n (yes/no)	2 / 99	0 / 51	2 / 48	0.24
HD, n (yes/no)	5 / 96	1 / 50	4 / 46	0.20
Cancer type, n (colorectal/gastric)	76 / 25	40 / 11	36 / 14	0.45
P-stage, n (0^a–2/3–4)	65 / 36	30 / 21	35 / 15	0.24
PNI	48.7 (44.2–53.2)	48.1 (43.4–52.8)	49.2 (45.1–53.4)	0.27
Albumin, g/dL	4.0 (3.7–4.3)	4.0 (3.6–4.3)	4.0 (3.8–4.3)	0.50
CRP, mg/dL	0.17 (0.06–0.34)	0.13 (0.05–0.24)	0.24 (0.08–0.49)	0.02
Hemoglobin, g/dL	12.8 (11.3–14.6)	12.5 (11.2–14.3)	13.3 (11.4–14.9)	0.49
WBC, $\times 10^3/\mu L$	6.2 (5.3–7.5)	6.1 (5.4–7.2)	6.4 (5.0–8.1)	0.90
TLC, $\times 10^3/\mu L$	1.6 (1.2–2.1)	1.5 (1.3–1.9)	1.7 (1.2–2.2)	0.35
PA, n (inactive/active)	34 / 67	13 / 38	21 / 29	0.07
Sedentary time, h/day	4 (3–7)	5 (3–7)	4 (2–7)	0.37
Grip strength, kg	28.3 (20.3–34.0)	23.8 (19.1–33.3)	28.6 (20.9–34.9)	0.40
Usual gait speed, m/s	1.25 (1.11–1.43)	1.24 (1.10–1.42)	1.28 (1.09–1.45)	0.47
6MWD, m	470 (405–547)	460 (370–510)	505 (431–572)	0.01

Surgical approach, n (open/laparoscopy)	52 / 49	24 / 27	28 / 22	0.75
Combined resection, n (yes/no)	22 / 79	7 / 44	15 / 35	0.04
Gall bladder, n (yes/no)	16 / 85	5 / 46	11 / 39	-
Other, n (yes/no)	7 / 94	3 / 48	4 / 46	-
Operative time, min	268 (201–334)	273 (210–330)	264 (193–339)	0.69
Blood loss, mL	60 (17–303)	91 (16–358)	59 (22–284)	0.89
Postoperative complications, n (yes/no)	25 / 76	12 / 39	13 / 37	0.77

Continuous variables are shown as median (interquartile range). Categorical variables were compared using the chi-squared test or Fisher's exact test. Continuous variables were compared using the Mann-Whitney U test.

[a], colorectal cancer only

BMI, body mass index; %VC, % vital capacity; FEV1.0%, forced expiratory volume in 1 second %; PS, performance status; DM, diabetes mellitus; CVD, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; HD, heart disease; P-stage, pathological stage; PNI, prognostic nutrition index; CRP, C-reactive protein; WBC, white blood cell count; TLC, total lymphocyte count; PA, physical activity; 6MWD, 6-minute walk distance

Table 2. Multivariate logistic regression analysis to predict postoperative functional recovery.

	Model 1		Model 2	
	OR (95% CI)	p value	OR (95% CI)	p value
PA, 0 = active 1 = inactive	3.115 (1.183–8.201)	0.02	3.812 (1.326–10.956)	0.01
6MWD, per 1 m	1.006 (1.002–1.011)	<0.01	1.006 (1.002–1.011)	<0.01
CRP, per 1.00 mg/dL	3.900 (1.332–11.413)	0.01	4.138 (1.383–12.377)	0.01
Combined resection, 0 = no 1 = yes	3.281 (1.082–9.949)	0.03	3.425 (1.101–10.649)	0.03

Four variables with $p<0.10$ (i.e., PA, 6MWD, CRP, and combined resection) in univariate analysis were entered into the multivariate logistic regression models.

Model 2 was adjusted for preoperative sedentary time.

OR, odds ratio; CI, confidence interval; PA, physical activity; 6MWD, 6-minute walk distance; CRP, C-reactive protein

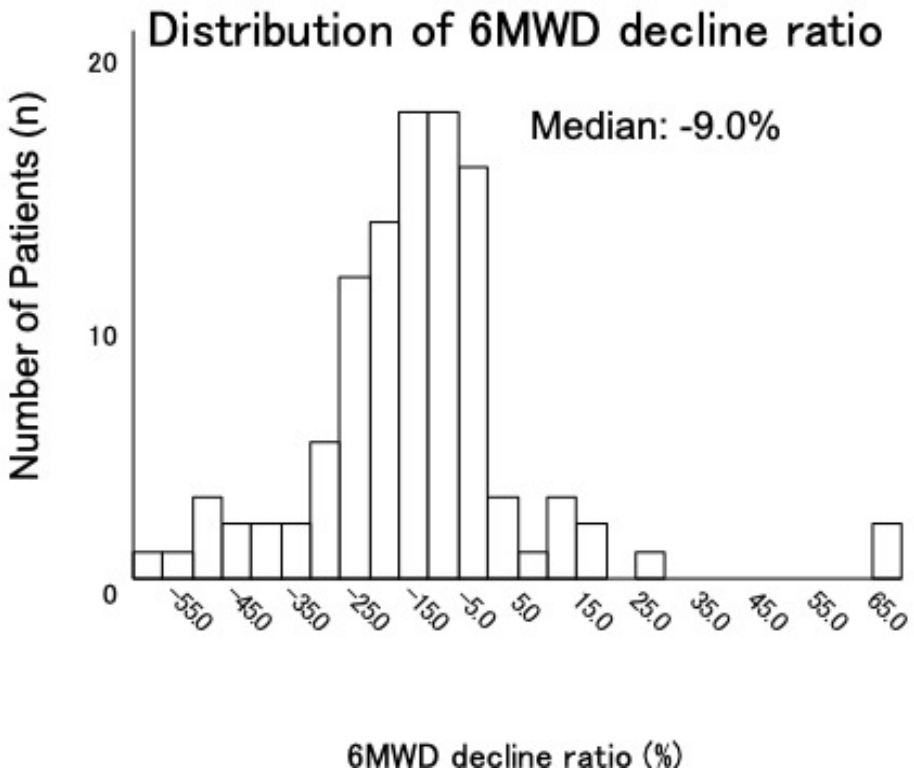

Figure 1. Distribution of the 6MWD decline ratio. The median of 6MWD decline ratio was -9.0 %.

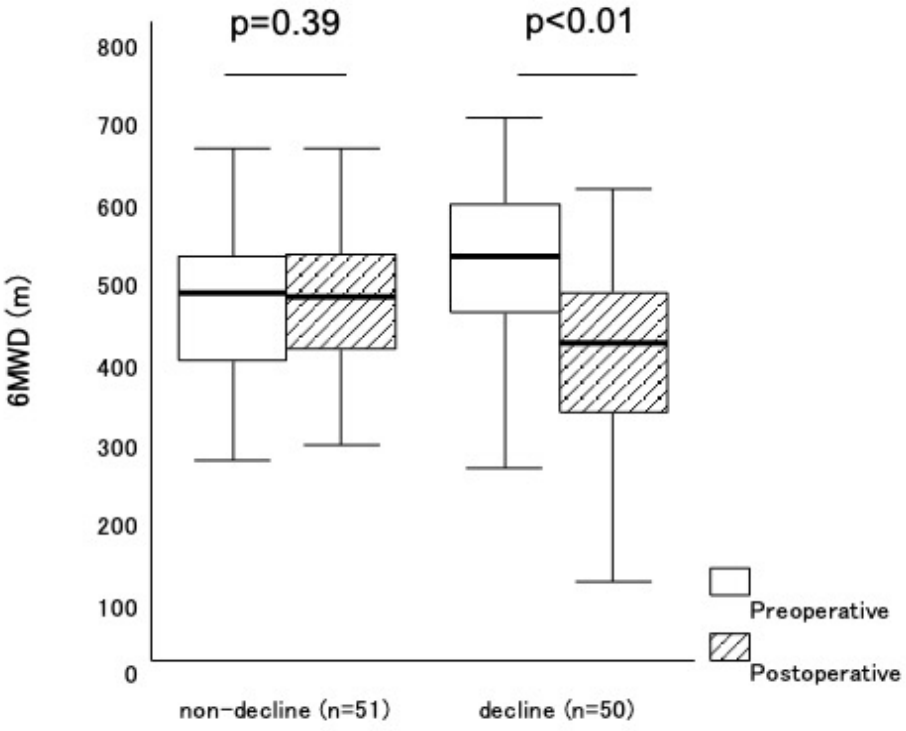

Figure 2. Changes in 6MWD in the non-decline group and the decline group. There was no significant decrease of 6MWD in the non-decline group [preoperative vs. postoperative: 460 (370–510) vs. 455 (390–510); p=0.39], but there was a significant decrease in the decline group [preoperative vs. postoperative: 505 (431–572) vs. 397 (308–462); p<0.01].

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