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Original Article

The association between objectively measured preoperative light-intensity physical activity and postoperative ambulation in patients with gastrointestinal cancer

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Abstract. [Purpose] To clarify the association between preoperative physical activity and postoperative ambulation based on physical activity intensity, and independent of functional capacity and depression, in patients with gastrointestinal cancer. [Participants and Methods] Seventy patients who underwent surgery for primary colorectal or gastric cancer were enrolled. Preoperative moderate-to-vigorous-intensity physical activity, light-intensity physical activity, and sedentary behavior were assessed using an accelerometer. The primary outcome was the days to postoperative first ambulation (capable of independently and continuously walking 150 m). Functional capacity and depression, as confounders, were evaluated by measuring the 6-minute walk distance and using the Hospital Anxiety and Depression Scale. [Results] Of the 70 patients, 28 had insufficient accelerometer data, and 42 were included in the analysis. Preoperative light-intensity physical activity, but not moderate-to-vigorous-intensity physical activity and sedentary behavior, was negatively associated with the days to postoperative first ambulation, after adjusting for age, preoperative functional capacity, and preoperative depression. [Conclusion] Preoperative light-intensity physical activity was associated with the days to postoperative ambulation independently of age, functional capacity, and depression. Hence, predicting delayed ambulation by preoperative light-intensity physical activity in patients with gastrointestinal cancer may be useful.

Key words: Gastrointestinal neoplasms, Exercise, Early ambulation

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INTRODUCTION

In patients with gastrointestinal cancer, delayed ambulation after major abdominal surgery has been associated with postoperative complications, postoperative length of hospital stay (LOS)[1)], and postoperative functional recovery[2)]. Generally, it is well known that performance status (PS), which reflects general condition[3)], affects adverse reactions to chemotherapy in patients with gastrointestinal cancer[4)]. Also, a previous study has reported that dynapenia (loss of muscle function) is related to chemotherapy-induced dose-limiting neurotoxicity in patients with gastrointestinal cancer[5)]. Therefore, it is important to identify modifiable factors of postoperative delayed ambulation that may cause delayed functional recovery to reduce chemotherapy toxicity related to physical function decline.

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Factors associated with delayed ambulation after gastrointestinal surgery include age, poor PS, emergency surgery, intraoperative fluid volume, laparotomy, and opioid use, with most reported as intraoperative factors[1, 6]. Furthermore, preoperative physical activity (PA), functional capacity assessed by the 6-minute walk distance (6MWD), and depression, which are modifiable factors and the focus of the rehabilitation field, have been reported to be associated with postoperative ambulation in other patients who underwent abdominal surgery[7–9]. These factors are reportedly related to each other[10–12]; however, no studies have been found that have examined their association with postoperative ambulation after excluding the influence of each factor. A detailed investigation of these relationships is particularly important in the rehabilitation field to prevent delayed ambulation.

A previous study showed that preoperative PA was associated with postoperative functional recovery in patients with gastrointestinal cancer[13]. Moreover, preoperative and postoperative steps have been moderately positively correlated in patients undergoing colorectal resection[14]. Therefore, it can be inferred that preoperative PA and postoperative ambulation are related in patients with gastrointestinal cancer and that postoperative delayed ambulation results in decreased postoperative PA and delayed functional recovery. In addition, studies investigating the relationship between preoperative PA and postoperative outcomes[13, 15] suggest that the association between preoperative PA and postoperative outcomes may vary according to the intensity of PA. However, there are no reports investigating the relationship between preoperative PA and postoperative ambulation in patients with gastrointestinal cancer, and it may be beneficial to investigate the impact of each PA intensity in developing interventions to prevent delayed ambulation after surgery.

Therefore, the purpose of the present study was to investigate whether preoperative PA by intensity is associated with the number of days to postoperative first ambulation independent of preoperative functional capacity and depression in patients with gastrointestinal cancer. We hypothesized that the relationship between the preoperative PA and the number of days to postoperative first ambulation would differ by the intensity of preoperative PA.

PARTICIPANTS AND METHODS

The design of this study is a prospective observational study. The present study enrolled consecutive 70 patients (51 males, 19 females; mean age: 68.6 ± 11.6 years) who underwent open or laparoscopic surgery for primary colorectal or gastric cancer between January 2019 and January 2022 at Kamiiida Daiichi General Hospital. Also, these patients had an independent activity of daily living (ADL) before admission to the hospital and on the day of the outpatient consultation, when the patients were informed of the surgery, they were explained that they were to wear an accelerometer. Exclusion criteria were defined as fewer than 5 days on which accelerometer data were obtained for more than 10 h/day. All patients underwent postoperative rehabilitation (twice a day on weekdays and once on Saturdays, a total of 40–60 min/day), which included ambulation, breathing exercises, and muscle strength exercises according to our institutional protocol. In addition, all patients practiced walking from the first postoperative day to achieve a continuous 150 m walk. This study was approved by the ethics committee of Kamiiida Daiichi General Hospital (approval number: 3009). Before participation, all patients were provided with a thorough explanation of the study and provided written consent based on the Declaration of Helsinki.

The number of days until the patient was able to walk 150 m continuously[16] (equivalent to one lap around the ward of our hospital) without assistance after surgery was defined as the number of days to postoperative first ambulation, and the evaluation was performed by physical therapists. Moreover, the median of the days to first postoperative ambulation was calculated; below the median was defined as early ambulation, and exceeding the median was defined as delayed ambulation. Reasons that resulted in delayed ambulation were also investigated using electronic medical records.

To investigate the impact of delayed ambulation on postoperative outcomes, the decline ratio of functional capacity, the incidence of postoperative complications, and postoperative LOS were evaluated. The decline ratio of functional capacity ([postoperative 6-minute walk distance {6MWD} − preoperative 6MWD] / preoperative 6MWD × 100 [%]) was calculated with reference to previous studies[17]. The 6MWD has been validated as a measure of postoperative functional recovery in patients undergoing gastrointestinal surgery[18, 19] and was measured according to guidelines[20]. The 6MWD was measured within 1 week before surgery (preoperative 6MWD) and 7 days after surgery (postoperative 6MWD). Postoperative complications were evaluated using Clavien–Dindo (CD) classification (grade 1−5)[21, 22]. In the present study, a CD grade ≥2 was defined as a postoperative complication.

Preoperative PA was measured using an accelerometer (Active Style Pro HJA-750C; Omron Healthcare, Kyoto, Japan). HJA-750C is the successor of HJA-350IT and has been reported for its principle and validity[23, 24]. The patient was lent an accelerometer at the time of surgical explanation at the gastrointestinal surgery outpatient clinic and instructed to wear it daily from the day after the loan until the day before admission, except when sleeping or during water-based activities, such as bathing, showering, and swimming. The accelerometer estimates PA intensity using metabolic equivalents (METs). PA intensity was classified as moderate to vigorous-intensity PA (MVPA) (≥3.0 METs), light-intensity PA (LPA) (>1.5 METs to <3.0 METs), and sedentary behavior (SB) (≤1.5 METs)[25]. The data were collected in 60-s epochs. The non-wear time was defined as no acceleration signal obtained for more than 60 min. Only accelerometer data for more than 5 valid days, with at least 10 wearing hours per day, were adopted, and the average duration of PA for each intensity was calculated and used for the analysis[26].

Confounders were selected based on the findings of previous studies. In surgical patients, it has been reported that preoperative 6MWD and depression have been associated with postoperative delayed ambulation[8, 9]. Also, it has been indicated that 6MWD and depression were related to PA[10, 11]. Therefore, the preoperative 6MWD and depression may be confounding factors in the relationship between preoperative PA and postoperative ambulation. Hence, investigating the relationship between preoperative PA and postoperative ambulation after adjusting for these confounders may assist in examining intervention methods. For evaluating preoperative depression, we used the Japanese version of the Hospital Anxiety and Depression Scale (HAD)[27, 28] within 1 week before surgery. The HAD consists of seven items each for the anxiety and depression subscales. A four-point response scale was used, with each subscale ranging from 0 to 21, with higher scores indicating more intense symptoms. Only depression scores (HAD-depression) were used in the present study.

Demographic factors, such as age, gender, and body mass index (BMI), were collected from medical records. In addition, the cancer site, pathological TNM stage, PS, comorbidity, surgical approach (laparotomy or laparoscopy), operative time, blood loss, and in/out balance were clinical factors. Albumin, C-reactive protein (CRP), and hemoglobin levels were collected to determine preoperative nutritional status, inflammation, and anemia. Anemia was defined as a hemoglobin level <13 g/dL in males, and <12 g/dL in females[29].

In statistical analysis, continuous and categorical variables are expressed as means ± standard deviation and the number of patients (%), respectively.

Multiple linear regression analysis was conducted to investigate the relationship between preoperative MVPA, LPA, and SB and days to first postoperative ambulation, adjusting for confounders. Model 1 was not adjusted; model 2 was adjusted for age; and model 3 was adjusted for age, preoperative 6MWD, and preoperative HAD-depression. The normality of the residuals was visually checked using multiple linear regression analysis. If preoperative PA indicators were associated with postoperative ambulation in Models 1 and 2 of the multiple linear regression analysis and the association disappeared in Model 3, it is possible that one or both of the 6MWD and HAD-depression, as confounders entered in Model 3, are mediators in the relationship between the PA indicator and postoperative ambulation. Therefore, if the association disappeared in Model 3, we checked whether the preoperative PA indicator or postoperative ambulation was associated with preoperative 6MWD or preoperative HAD-depression. Once a significant relationship was confirmed between the PA indicator and the postoperative ambulation, one each of 6MWD and HAD-depression was entered for the association between the PA indicator and the postoperative ambulation, and if the association between the PA indicator and the postoperative ambulation disappeared, the entered variable was determined to be a mediator.

Moreover, to investigate the effect of postoperative delayed ambulation on the postoperative course, we compared the decline ratio of functional capacity, the incidence of postoperative complications, and postoperative LOS between the delayed ambulation group and the early ambulation group using the Mann–Whitney U test for continuous variables and the χ^2 test for categorical variables.

Referring to studies showing the relationship between objectively measured preoperative PA and the number of days to return to the same ADL as before surgery[30], which reflects functional recovery after surgery, the sample size was set to a minimum of 31 cases, and finally to 40 cases considering the number of variables to be entered into multiple linear regression analysis. All statistical analyses were performed using EZR version 1.61 (Saitama Medical Center, Jichi Medical University, Shimotsuke, Japan)[31], and statistical significance was set at $p<0.05$.

RESULTS

Of the 70 patients, 28 had insufficient accelerometer data and 42 were included in the analysis (Fig. 1). Table 1 shows the characteristics of the included patients. For included patients, the mean age was 68.2 ± 12.0 years, the number of males was 28 (66.7%), the number of patients with colorectal cancer was 32 (76.2%), and the number of patients with PS 0 was 40 (95.2%). The mean MVPA time was 39.0 ± 30.4 min/day, the mean LPA time was 302.7 ± 103.3 min/day, and the median SB was 439.4 ± 160.2 min/day.

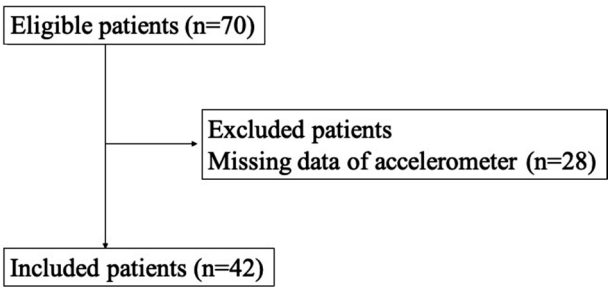

Fig. 1. Flow chart of patient selection.

Table 1. Included patient characteristics

	n=42
Age, years	68.2 ± 12.0
Gender, n (%)	
Male	28 (66.7)
Female	14 (33.3)
BMI, kg/m^2	22.3 ± 2.9
Cancer site, n (%)	
Colorectal	32 (76.2)
Gastric	10 (23.8)
Stage, n (%)	
0	4 (9.5)
1	11 (26.2)
2	14 (33.3)
3	12 (28.6)
4	1 (2.4)
PS, n (%)	
0	40 (95.2)
1	2 (4.8)
Comorbidity, n (%)	
DM	8 (19.0)
HD	6 (14.3)
CVD	3 (7.1)
COPD	1 (2.4)
Albumin, g/dL	4.2 ± 0.3
CRP, mg/dL	0.36 ± 0.94
Anemia, n (%)	13 (31.0)
6MWD, m	494.2 ± 107.6
HAD-depression, point	5.9 ± 3.9
MVPA time, min/day	39.0 ± 30.4
LPA time, min/day	302.7 ± 103.3
SB time, min/day	439.4 ± 160.2
Intraoperative characteristics	
Surgical approach, n (%)	
Open	12 (28.6)
Laparoscopy	30 (71.4)
Combined resection, n (%)	6 (14.3)
Operative time, min	281.5 ± 81.4
Blood loss, mL	104.1 ± 167.9
In/out balance, mL	1,447.5 [456.1]
Postoperative characteristics	
Days to first ambulation, days	2.7 ± 1.6
Decline ratio of functional capacity, %	−17.4 ± 16.1
Postoperative complications, n (%)	18 (42.9)
Postoperative LOS, days	13.3 ± 9.9

Continuous variables are shown as means ± standard deviation and categorical variables are shown as numbers (%).
BMI: body mass index; PS: performance status; DM: diabetes mellitus; HD: heart disease; CVD: cerebrovascular disease; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; 6MWD: 6-minute walk distance; HAD: Hospital Anxiety and Depression Scale; MVPA: moderate-to-vigorous-intensity physical activity; LPA: light-intensity physical activity; SB: sedentary behavior; LOS: length of hospital stay.

Table 2 shows the results of the multiple regression analysis to investigate the relationship between preoperative MVPA, LPA, and SB and days to postoperative first ambulation adjusted for confounders. Preoperative LPA was associated with days to postoperative first ambulation adjusted for age, preoperative 6MWD, and preoperative HAD-depression (β=−0.583, B=−0.005 [95% confidence interval {CI} −0.009, −0.001], p=0.012). On the other hand, preoperative MVPA was related to days to postoperative first ambulation adjusted for age, but not related adjusted for age, preoperative 6MWD, and preoperative HAD-depression (β=−0.371, B=−0.012 [95% CI −0.032, 0.007], p=0.226). Moreover, SB was not associated before and after adjusting for confounders (β=0.299, B=0.001 [95% CI −0.001, 0.004], p=0.224).

Table 3 shows the results of an investigation of whether preoperative 6MWD and HAD-depression could mediate the relationship between preoperative MVPA and postoperative ambulation. Preoperative MVPA was associated with postoperative ambulation adjusted for age only (B=−0.020 [95% CI −0.040, −0.000], p=0.040). Preoperative 6MWD and HAD-depression were related to postoperative ambulation (B=−0.007 [95% CI −0.013, −0.001], p=0.012 and B=0.130 [95% CI 0.003, 0.257], p=0.045, respectively). On the other hand, preoperative MVPA was associated with HAD-depression (B=−0.051 [95% CI −0.098, −0.004], p=0.033), but not associated with 6MWD (B=0.757 [95% CI −0.308, 1.823, p=0.158]. The association between preoperative MVPA and postoperative ambulation disappeared when adjusted for preoperative HAD-depression (B=−0.015 [95% CI −0.036, 0.004], p=0.133).

After dividing the patients into two groups based on the median number of days to the first postoperative ambulation (median was 2 days), 19 patients were assigned to the delayed ambulation group (exceeding 2 days). The delayed ambulation group tended to have a higher decline ratio in functional capacity than the early ambulation group (−21.3 ± 14.8% vs. −14.4 ± 16.7%, p=0.074). No significant differences were observed in the incidence of postoperative complications and postoperative LOS between the two groups (p>0.999 and p=0.383, respectively) (Table 4). The most common reason for postoperative delayed ambulation was pain (42.1%), and the second was the need for assistance due to decreased balance (21.0%) (Table 5).

Table 2. The association between preoperative PA and postoperative ambulation adjusted for confounders

Independent factor	Model	β (95% CI)	B (95% CI)	SE	p
MVPA, per 1 min/day	1	−0.506 (−0.997, −0.016)	−0.016 (−0.032, −0.000)	0.007	0.043*
	2	−0.628 (−1.228, −0.028)	−0.020 (−0.040, −0.000)	0.009	0.040*
	3	−0.371 (−0.982, 0.240)	−0.012 (−0.032, 0.007)	0.009	0.226
LPA, per 1 min/day	1	−0.686 (−1.154, −0.219)	−0.006 (−0.011, −0.002)	0.002	0.005*
	2	−0.679 (−1.153, −0.205)	−0.006 (−0.011, −0.001)	0.002	0.006*
	3	−0.583 (−1.030, −0.135)	−0.005 (−0.009, −0.001)	0.002	0.012*
SB, per 1 min/day	1	0.398 (−0.101, 0.899)	0.002 (−0.000, 0.005)	0.001	0.115
	2	0.387 (−0.120, 0.896)	0.002 (−0.000, 0.005)	0.001	0.131
	3	0.299 (−0.191, 0.790)	0.001 (−0.001, 0.004)	0.001	0.224

Model 1 was not adjusted, Model 2 was adjusted for age, and Model 3 was adjusted for age, 6MWD, and HAD-depression.
*p<0.05.
PA: physical activity; CI: confidence interval; SE: standard error; MVPA: moderate-to-vigorous-intensity physical activity; LPA: light-intensity physical activity; SB: sedentary behavior; 6MWD: 6-minute walk distance; HAD: Hospital Anxiety and Depression Scale.

Table 3. Investigation of whether preoperative 6MWD and HAD-depression are the mediators of the association between preoperative MVPA and postoperative ambulation

Model	Dependent variable	Independent variable	B (95 % CI)	SE	p
1	Days to postoperative first ambulation	MVPA	−0.020 (−0.040, −0.000)	0.009	0.040*
2	6MWD	MVPA	0.757 (−0.308, 1.823)	0.527	0.158
3	Days to postoperative first ambulation	6MWD	−0.007 (−0.013, −0.001)	0.002	0.012*
4	HAD-depression	MVPA	−0.051 (−0.098, −0.004)	0.023	0.033*
5	Days to postoperative first ambulation	HAD-depression	0.130 (0.003, 0.257)	0.062	0.045*
6	Days to postoperative first ambulation	MVPA	−0.015 (−0.036, 0.004)	0.010	0.133

Models 1–5 were adjusted for age, and Model 6 was adjusted for age and HAD-depression.
*p<0.05.
CI: confidence interval; SE: standard error; MVPA: moderate-to-vigorous-intensity physical activity; 6MWD: 6-minute walk distance; HAD: Hospital Anxiety and Depression Scale.

Table 4. The comparison of secondary outcomes between patients with early ambulation and delayed ambulation

	Early ambulation (n=23)	Delayed ambulation (n=19)	p
Decline ratio of functional capacity, %	−14.4 ± 16.7	−21.3 ± 14.8	0.074
Postoperative complications, n (%)	10 (43.5)	8 (42.1)	>0.999
Postoperative LOS, days	12.5 ± 8.8	14.3 ± 11.4	0.383

Continuous variables are shown as means ± standard deviation and categorical variables as numbers (%).
LOS: length of hospital stay.

Table 5. The reasons for postoperative delayed ambulation

n=19	n (%)
Pain	8 (42.1)
Needed assistance due to decreased balance	4 (21.0)
Fatigue	3 (15.7)
Dyspnea	3 (15.7)
Nausea	1 (5.2)

DISCUSSION

The main finding of the present study was that preoperative LPA, but not MVPA or SB, was associated with the days to first postoperative ambulation adjusted for age, functional capacity, and depression. To our knowledge, this is the first study to examine the relationship between the days to postoperative first ambulation and preoperative PA by activity intensity, indicating that even in patients with high preoperative functional capacity and no depressive tendencies, those with low preoperative LPA may have postoperative delayed ambulation.

There are several possible mechanisms through which preoperative LPA is associated with postoperative ambulation. In this study, one of the main reasons for delayed ambulation was the need for assistance due to decreased balance, and the median age of the included patients was 68 years. It has been shown that LPA was more associated with gait function than MVPA in adults over 70 years of age[32]. Therefore, it is possible that LPA was more associated with gait function than MVPA in this study, too, and patients with less LPA may have poor gait function and be prone to even poorer postoperative gait function. In addition, previous studies have indicated that LPA measured by an accelerometer is positively related to pain inhibitory function in older adults[33], and an association has been shown between postoperative pain management and postoperative ambulation in patients undergoing abdominal surgery[6]. The present study indicated that pain was the most common reason for postoperative delayed ambulation. Therefore, patients with less preoperative LPA are more likely to experience more postoperative pain and may be more likely to delay postoperative ambulation. In the elderly, LPA is performed much more often than MPVA during a day of activity[11], and preoperative patients may have more difficulty performing MVPA due to symptoms associated with the disease. Therefore, in patients with gastrointestinal cancer, especially elderly patients, increasing preoperative LPA to prevent postoperative delayed ambulation is possible to be relatively easier to conduct and may play an important role.

Our results showed that preoperative MVPA was associated with postoperative ambulation adjusted for age only but was not associated with adjustment for age, preoperative functional capacity, and depression. Moreover, preoperative HAD-depression, but not 6MWD, was related to preoperative MVPA and postoperative ambulation, and the relationship between preoperative MVPA and postoperative ambulation disappeared after adjustment for preoperative HAD-depression. These results suggest that depression mediates the association between preoperative MVPA and postoperative ambulation. Paolucci et al. reported that moderate- and vigorous-intensity exercise has been effective in reducing depressive symptoms[34] and increasing MVPA might be a useful intervention to prevent postoperative delayed ambulation in patients with preoperative depressive tendencies. In addition, preoperative SB was not correlated with postoperative ambulation before and after adjusting for 6MWD and HAD-depression in the present study, and patients with delayed ambulation tended to have a higher decline ratio in postoperative functional capacity than those with early ambulation. Our previous study indicated that preoperative PA, but not SB, was associated with postoperative functional recovery[13], and the results of the present study may complement those of our previous study.

de Almeida has reported that postoperative functional capacity was higher in patients with early ambulation than in those with delayed ambulation[2]. Furthermore, a significantly higher incidence of postoperative complications has been reported in patients with delayed ambulation compared with early ambulation[1], and it was known that postoperative complications prolonged postoperative LOS in gastrointestinal surgery patients[35, 36]. On the other hand, in the present study, the decline

ratio of functional capacity tended to be higher in patients with postoperative delayed ambulation than in those with postoperative early ambulation, whereas the incidence of postoperative complications and postoperative LOS did not differ between patients with early ambulation and delayed ambulation. The difference from the previous study might be attributed to the different definitions of postoperative ambulation. In this study, postoperative ambulation was defined as the ability to walk 150 m continuously without assistance, which is considered to require a higher ability than the definition in previous studies[1, 6, 8]. Therefore, even patients who were judged to have delayed ambulation in this study were able to ambulate earlier than in the previous studies, and as a result, there was no significant difference in the incidence of postoperative complications or postoperative LOS between the early and delayed ambulation groups. In addition, postoperative complications have been reported to affect postoperative functional recovery[37], but in this study, there was no difference in the incidence of postoperative complications between the early and delayed ambulation groups, suggesting that the delayed ambulation group tended to have delayed recovery of postoperative functional capacity due to the decreased PA associated with delayed ambulation.

We consider that preoperative LPA could be useful as an indicator of the degree of postoperative ambulation and an increase in preoperative LPA would be an effective method to prevent postoperative delayed ambulation in gastrointestinal cancer patients.

The present study had several limitations. First, the sample size was too small to adjust for other confounders and fully investigate the relationship between postoperative delayed ambulation and postoperative outcomes. However, this is the first study to investigate the relationship between objectively measured PA and postoperative ambulation, which is a strength of the present study. Second, because this study included only patients with PS of 0 or 1, the results of this study may not apply to patients who tend to be in poor general condition. Finally, the most common cause of delayed ambulation is pain, yet the degree of pain at the time of ambulation is not evaluated by scale.

There is one implication for future study. In a systematic review of randomized controlled trials comparing PA levels between groups that used accelerometers and those that did not, it was reported that the groups that used accelerometers had more PA than those that did not[38]. Therefore, when conducting research using accelerometers, it would provide more reliable data if it is possible to devise ways to blind participants to the fact that they are wearing accelerometers.

In conclusion, preoperative LPA was associated with the days to postoperative first ambulation, independent of age, functional capacity, and depression, whereas MVPA and SB were not associated with ambulation in patients with gastrointestinal cancer.

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Conflict of interest

None.

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