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Original Article

Effect of preoperative physical activity on postoperative outcomes in esophageal cancer

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Abstract. [Purpose] This study aimed to examine the characteristics of preoperative physical activity and its impact on the postoperative period in patients who underwent surgery for esophageal cancer. [Participants and Methods] The participants were 30 patients who were diagnosed with esophageal cancer, underwent surgery, and fulfilled their conditions. Preoperative physical activity was measured using the step count, and metabolic equivalents as the amount of physical activity. We examined the relationships between preoperative step count and METs, patient demographics, treatment-related factors, preoperative physical function, and activities of daily living. Moreover, we examined the relationships of preoperative step count and METs with postoperative mobilization, physical activity, physical function, and activities of daily living. [Results] Preoperative step count was related to age, Glasgow prognostic score, and preoperative functional independence and associated with step count on postoperative days 7–13, METs on postoperative days 7–9, 6-min walking distance, and functional independence measures at discharge. [Conclusion] Improving the nutritional status and increasing preoperative physical activity by walking for esophageal cancer may help improve physical activity after postoperative day 7, exercise tolerance, and activities of daily after discharge.

Key words: Esophageal cancer, Physical activity, Step count, METs

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INTRODUCTION

Esophageal cancer is more common in men and occurs most often in people in their 60s and 70s, and drinking and smoking are considered risk factors. The incidence of esophageal cancer in Japan is increasing for men but remains unchanged for women[1]. The mortality rates have remained stable for men but decreasing for women[2]. While the 5 year survival rate is 62% for cancer in general, it is 40.6%[3] for esophageal cancer. The 10 year survival rate is 66.9% for cancer, but it is 45.9%[4] for esophageal cancer. Therefore, esophageal cancer has a lower-than-average survival rate.

The treatment for esophageal cancer includes endoscopic resection, surgery, radiotherapy, and chemotherapy, which are selected depending on the disease stage and general condition. Surgery for esophageal cancer is highly invasive, and the postoperative complication and surgery-related mortality rates are higher than those of other diseases[5–7]. Respiratory complications have a relatively high incidence after surgery for esophageal cancer[6, 8], and they are the main postoperative cause of death[9]. In addition, it has been reported that physical function and activities of daily living (ADLs) decline after surgery in patients with gastrointestinal cancers and not just those with esophageal cancer[10, 11]. Therefore, it is important to prevent postoperative complications, including those related to the respiratory system and disuse syndrome, during perioperative rehabilitation for esophageal cancer.

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Before surgery, prehabilitation is performed. Prehabilitation is an intervention to promote physical and mental health to prevent the occurrence or aggravation of disorders that may occur due to treatment[12)]. For esophageal cancer, performing intensive pulmonary rehabilitation before surgery reduces the incidence of postoperative respiratory complications[13)]. It has been reported that early mobilization is associated with the incidence of postoperative respiratory complications[14)], and preoperative pulmonary rehabilitation and early postoperative mobilization are recommended.

In addition, guidance is provided to maintain and improve physical activity before surgery. Patients with esophageal cancer who developed postoperative respiratory complications had lower preoperative physical activity than those who did not. Furthermore, preoperative physical activity influences the development of postoperative respiratory complications[15)]. However, the effect of preoperative physical activity on postoperative mobilization, physical function, and ADLs in patients with esophageal cancer has not been clarified.

Therefore, the purpose of this study was to examine the effect of preoperative physical activity of esophageal cancer on postoperative mobilization, physical activity, physical function, and ADLs. The results of this survey may help provide evidence to maintain and improve physical activity before surgery as part of perioperative rehabilitation for esophageal cancer. First, we examined the association of preoperative physical activity with patient background, treatment, preoperative physical function, and ADLs. We subsequently examined its relationship with postoperative mobilization, physical activity, physical function, and ADLs.

PARTICIPANTS AND METHODS

The study initially included 53 patients who underwent surgery for esophageal cancer at Teine Keiinkai Hospital from January 1, 2022, to August 31, 2023, and received intervention from a physical therapist at least one week before surgery. The exclusion criteria were difficulty walking and insufficient data. Twenty-three patients with incomplete data due to not wearing the activity meter or wearing it for less time before or after surgery were excluded, and finally 30 patients were included (Fig. 1). The study design was a prospective observational study. The study items included patient background and treatment-related data, physical function, ADLs, physical activity, and progress.

The collected patient demographic and treatment-related data were as follows: age, gender, body mass index (BMI), pulmonary function test (VC, %VC, FEV, FEV1.0%), nutritional status, tumor progression, neoadjuvant therapy, postoperative complications, days of preoperative rehabilitation, and length of hospital stay. Nutritional status was determined using the Glasgow Prognostic Score (GPS). Glasgow Prognostic Score is a nutritional evaluation method that is related to the prognosis of cancer[16)]. It also reflects cancer cachexia[17)]. For postoperative complications, we used the Clavien–Dindo (CD) classification, which covers all postoperative complications and deals with adverse events. The CD classification is divided into seven levels of severity from Grades I to V. Grade I represents a state that is a deviation from the normal postoperative course but does not require drug therapy, surgical treatment, endoscopic treatment, or interventional radiology treatment. Grade I cases were judged to have no postoperative complications. Grade II or higher cases were judged to have postoperative complications. Regarding surgery, the duration of surgery and blood loss were measured.

Physical function was assessed as muscle strength, frailty, and exercise tolerance. Muscle strength was measured as grip strength, which is an index of whole-body strength, and knee extension strength, which is an index of ADLs and movement. Grip strength was measured using a digital grip dynamometer (TKK-5401; Takei Scientific Instruments Company Limited, Niigata, Japan). The measurement order was as follows: dominant hand → non-dominant hand → dominant hand → non-

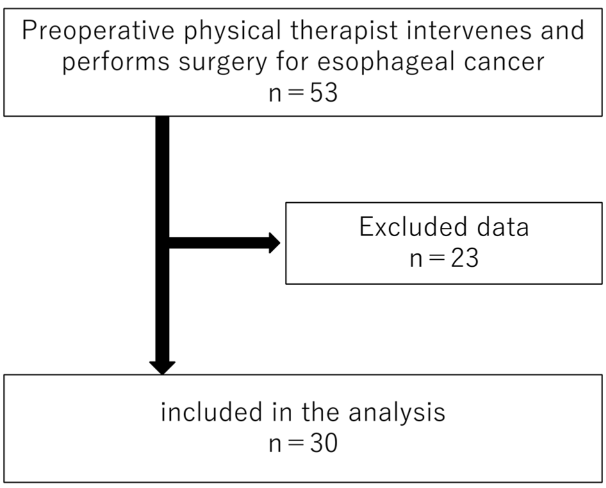

Fig. 1. Extracted data flow.

dominant hand. The measurements were taken on the left and right sides, and the highest was used as the grip strength. In addition, knee extension muscle strength was measured using a handheld dynamometer (Mobie MT-100; SAKAI Medical Company Limited, Tokyo, Japan). The output of the results was set to N (Newton), and the distal lower leg was fixed to the chair with a belt while sitting in a chair position. With the knee flexed at 90°, the knee joint extension was measured twice (alternating between left and right) by gradually applying force until it reached the maximum, and the maximum value was taken. In addition to the muscle strength value (N), the lever arm was measured, and the body weight ratio (%) was calculated. The revised J-CHS criteria were used for frailty assessment. The revised J-CHS standards evaluated the following five items: (a) weight loss: those who answered "yes" to "Have you experienced (unintentional) weight loss of 2 kg or more in the past 6 months?"; (b) grip strength: measured with the dominant hand for men under 28 kg and women under 18 kg; (c) fatigue: those who answered "yes" to "I feel tired for no reason (over the past two weeks);" (d) normal walking speed: less than 1.0 m/sec; and (e) activity amount: those who answered "I don't do any exercise or gymnastics" to "How many days a week do you do light exercise (including farm work)?" or "How many days a week do you do regular exercise/sports (including farm work)?"

Items (a), (c), and (e) were question-type items, and items (b) and (d) were measurement-type items. To measure normal walking speed, a 1-m run-up path was set up before and after the measurement section, and the time for the 5-m measurement section was measured. Those who met three or more of the five evaluation criteria were classified as frail. Those who met one or two of the criteria were considered prefrail, and those who did not meet either of the criteria were considered healthy or robust. For exercise tolerance, the distance of the 6-minute walking test (hereinafter referred to as 6-minute walking distance; 6MWD) was used. During the 6-minute walk test, the participants were instructed to walk as long as possible, and measurements were made by uniformly speaking to them to ensure a constant load. The participants were also instructed to lean against a wall if they needed to take a break and rest as needed. SpO_2, dyspnea, fatigue, and walking distance were assessed before and after walking, and only the walking distance was used.

The Functional Independence Measure (FIM) was used to evaluate ADLs. When assessing physical function and ADLs, muscle strength, frailty, exercise tolerance, and ADLs were evaluated preoperatively, and muscle strength, exercise tolerance, and ADLs were evaluated upon discharge.

A triaxial accelerometer activity meter (HJA-750C Active style Pro; OMRON Corporation, Kyoto, Japan) was used to measure the amount of physical activity. The data collected were step count, walking time (minutes), calories burned (kcal), METs, and activity time, and data were recorded every 10 s. In this study, we adopted step count as an indicator of walking, which is taught in clinical practice, and METs, which applies to various activities other than walking, as intensity. The attachment site was the lower back for everyone. During the wearing period, the activity meter was given to the participant during preoperative rehabilitation and collected upon admission to the hospital the day before surgery. Measurements were resumed when the patient entered the intensive care unit (ICU) on postoperative day 1, and the activity meter was collected upon discharge. The preoperative data were collected from the preoperative rehabilitation implementation until admission on the day before surgery, and the postoperative data were collected from postoperative day 1 to the time of discharge. The preoperative data were average values for one week excluding the day before hospitalization for surgery; after surgery, daily values from 9:00 a.m. to 5:00 p.m. up to postoperative day 14 and values at the time of discharge were used. Items related to postoperative mobilization included the date of postoperative mobilization, the date of starting to walk, and the date of independent walking.

In addition, perioperative rehabilitation by a physical therapist was provided to all patients before surgery. In the preoperative period, breathing exercises using an incentive spirometry (Coach 2; Smiths Medical Japan Corporation, Tokyo, Japan) and postoperative directed cough were taught as respiratory rehabilitation, and the necessity of early mobilization from bed after surgery was explained. In the postoperative period, early mobilization and exercise therapy were implemented from the first postoperative day.

For statistical analysis, we first examined the relationships between preoperative step count, METs, patient background, treatment-related factors, physical function, and ADLs using Pearson's product moment and Spearman's rank correlation coefficients. Next, we examined the relationship between the preoperative step count and METs and postoperative mobilization, physical activity, physical function, and ADLs using Pearson's product moment and Spearman's rank correlation coefficients. For statistical analysis, we used IBM SPSS Statistics Version 21 (IBM Japan, Tokyo, Japan). The significance level was set at 5%.

This study was conducted with the approval of the Keijinkai Medical Corporation Teine Keijinkai Hospital Ethics Committee (management number 2-021300-00). Similarly, this study was approved by the Hirosaki University Graduate School of Health Sciences Ethics Committee (reference number 2021-057). The purpose and methods of this study were fully explained to the participants, and each of them provided written informed consent.

RESULTS

Table 1 shows the demographic characteristics and treatments of the patients. The mean age of the participants was 69.9 ± 8.8 years. Twenty-one were males and 9 were females. Nutritional status was good with a mean GPS of 0.2 ± 0.4. More than half of the 17 patients received neoadjuvant therapy. Postoperative complications were observed in 10 patients with

CD classification Grade II or higher. The preoperative step count was 3,705.6 ± 2,229.9 steps, and the preoperative METs was 1,152.9 ± 552.1. Table 2 shows the changes in physical function of the participants and ADLs, and Table 3 shows the postoperative mobilization.

Regarding the preoperative physical activity and patient background and treatment-related factors, the preoperative step count was correlated with age ($r=-0.407$, $p<0.05$) and GPS ($r=-0.375$, $p<0.05$). Furthermore, no relationship was observed with the preoperative METs.

The preoperative step count was correlated with preoperative FIM ($r=0.418$, $p<0.05$). There was no correlation between preoperative step count and METs related to physical function. The preoperative step count was correlated with step count from postoperative day 7 to 13 and at discharge and also correlated with METs from postoperative day 7 to 9. Furthermore,

Table 1. Patients characteristics

	All patients N=30
Age, years, mean ± SD	69.9 (8.8)
Gender, n (%)	
Male	21 (70)
Female	9 (30)
BMI, kg/m^2, mean ± SD	21.8 (3.5)
Preoperative pulmonary function tests, mean ± SD	
VC, L	3.3 (0.9)
VC, %pred	106.1 (23.7)
FEV_1, L	7.5 (19.4)
FEV_1, %pred	77.7 (14.1)
GPS, mean ± SD	0.2 (0.4)
Revised J-CHS criteria, mean ± SD	1.6 (1.2)
stage, n (%)	
1	10 (33)
2	10 (33)
3	8 (27)
4	2 (7)
Neoadjuvant therapy, n (%)	17 (57)
Operation time, min, mean ± SD	501.9 (109.2)
Blood loss, mL, mean ± SD	137.0 (103.3)
CDC grade ≥II, n (%)	10 (33)
Physical activity	
Preoperative step count, steps, mean ± SD	3,705.6 (2,229.9)
Preoperative METs, mean ± SD	1,152.9 (552.1)
Preoperative rehabilitation days, days, mean ± SD	22.4 (17.6)
LOS, days, mean ± SD	23.6 (9.0)

SD: standard deviation; BMI: body mass index; VC: vital capacity; FEV1: forced expiratory volume in one second; GPS: glasgow prognostic score; J-CHS: Japanese version of the cardiovascular health study; CDC: Clavien–Dindo classification; METs: metabolic equivalents; LOS: length of stay.

Table 2. Patients physical function and activity of daily living (ADL)

	Preoperative	Discharge
Hand grip strength, kg	28.5 (9.5)	28.7 (8.2)
QF, N	306.0 (112.2)	281.5 (103.4)
QF, %	66.4 (17.7)	65.1 (18.2)
6MWD, m	463.5 (93.6)	408.3 (87.5)
FIM	123.4 (5.6)	123.8 (3.6)

Mean ± SD.
QF: quadriceps femoris muscle force; 6MWD: 6-minute walking distance; FIM: functional independence measure; SD: standard deviation.

Table 3. Patients mobilization status

	Mean ± SD
Start date of mobilization*, day	1.1 (0.3)
Start date of gait, day	1.3 (0.5)
Gait independence, day	6.3 (2.5)

*The start date of mobilization was the day the patient left the bed (including standing).
SD: standard deviation.

the step count before surgery was correlated with 6MWD (r=0.470, p<0.01) and FIM (r=0.521, p<0.01) at the time of discharge. The preoperative METs had no relationship with postoperative mobilization, physical activity, physical function, or ADLs.

DISCUSSION

This study targeted patients undergoing surgery for esophageal cancer. We examined preoperative physical activity and its effect on patient background, treatment, postoperative mobilization, physical activity, physical function, and ADLs. The amount of physical activity was determined using the step count and METs. The preoperative step count was associated with age and GPS, and the preoperative physical function and ADLs were associated with FIM. In addition, the preoperative step count was associated with step count from postoperative day 7 to 13, METs from postoperative day 7 to 9, and 6MWD and FIM at discharge. The preoperative METs were not associated with patient characteristics, treatment-related items, preoperative or postoperative mobilization, physical activity, physical function, or ADLs.

The preoperative step count was associated with age, GPS, and FIM. First, regarding the relationship with age, Higuchi et al. measured ADLs in young and older adults using a pedometer with a built-in acceleration sensor. The total step count, total energy consumption, and amount of exercise per day of older adults were lower than those of younger people[18], and aging was thought to affect the relationship between the step count before surgery and age in the present study. Next, regarding the relationship with GPS, which is an indicator of nutritional status, an increase in physical activity leads to an increase in energy consumption, so it was thought that physical activity is related to nutritional status. Furthermore, GPS is an index reflecting cancer cachexia[17]. Additionally, more than half of the participants received chemotherapy as neoadjuvant therapy. Common side effects of chemotherapy include nausea, vomiting, fatigue, and loss of appetite. Therefore, the nutritional status may have been affected. However, the present study was not able to verify this, as with cancer cachexia, and further verification is required in the future.

Furthermore, no relationship was found between preoperative step count and METs regarding postoperative complications, which are considered important in the perioperative period. Feeney et al. showed that patients with esophageal cancer who developed postoperative respiratory complications had higher preoperative physical activity than those who did not. Furthermore, they reported that preoperative physical activity influenced the development of postoperative respiratory complications[15]. These are different from the results of the present study. In previous studies, the preoperative intervention was unclear, but in the present study, all participants underwent preoperative pulmonary rehabilitation. Preoperative pulmonary rehabilitation, which has been reported to be effective, may affect the development of postoperative respiratory complications.

Regarding preoperative physical function, no relationship was found between preoperative step count and METs with grip strength, knee extension muscle strength, 6MWD, or any item of the revised J-CHS criteria. A relationship between physical activity level and muscle strength was reported by previous studies[19–21], but no relationship was found in this study. It differs from previous studies in that the participant of this study is cancer disease. Therefore, the effect of cancer-specific cancer cachexia was considered. The participants also included those receiving chemotherapy as neoadjuvant therapy. Chemotherapy causes abnormal mitochondrial function in skeletal muscle, increases oxidative stress, and reduces muscle contractility and endurance[22]. Nakano and Ishii reported that cancer patients undergoing chemotherapy and radiotherapy are characterized by a mismatch between muscle volume and muscle strength[23]. Therefore, for grip strength and knee extension muscle strength, it was thought that there was no relationship between preoperative step count and METs due to the influence of the disease or treatment. 6-minute walking distance is the result from the 6-minute walk test, and the 6-minute walk test is related to lower limb muscle strength[24, 25]. Since muscle strength is also included in the evaluation items of the revised J-CHS criteria, it was thought that the results were influenced by the disease and treatment.

Regarding postoperative mobilization and physical activity, relationships were observed between the preoperative step count and the step count and METs after postoperative day 7. After surgery, efforts are made to prevent postoperative complications including respiratory problems and disuse syndrome. In clinical practice, the diaphragm and lung function are affected in the supine position, because the abdominal organs push the diaphragm toward the head to prevent respiratory complications[26–28]. To encourage the expectoration of secretions from the airways, it is recommended that the patient initially sits, including in a head-up position[29]. In addition, breathing exercises are promoted, and physical activities such as walking and exercise are encouraged in terms of motor function and ability. Postoperative data on the step count and METs showed that the amount of physical activity increased over time. However, it was thought that refilling had an effect, given that it was not related to physical activity by postoperative day 7. Refilling refers to the movement of body fluid components from the interstitium into blood vessels, and when a surgical invasion is applied to the body, the permeability of microvessels increases, and plasma components leak into the interstitium. Depending on the degree of surgical invasion, vascular permeability normalizes approximately 24–72 hours after surgery, and water that has leaked out of the blood vessels returns to the blood vessels. If the renal function of the patient is maintained, an increase in urine output and blood pressure may be observed, but this will not significantly affect the course of the disease. However, when a large amount of water accumulates in blood vessels, it affects breathing and circulatory dynamics, leading to the development of pulmonary edema and heart failure. During the early postoperative period, breathing and hemodynamics may become unstable, and refilling may worsen the condition. Therefore, it was thought that refilling may have affected postoperative physical activity. It is also possible that symptoms such as postoperative pain were involved, but this could not be verified in this study. Furthermore, preoperative step count was more correlated with step count than postoperative METs. After surgery, walking is the main activity that can be undertaken in the hospital environment to promote physical activity from an early stage to prevent complications. In other words, this was thought to reflect walking as an improvement in physical activity before surgery.

A relationship was observed between preoperative step count and 6MWD and FIM at discharge. Agmon et al. reported that 900 steps per day taken by older hospitalized patients was significantly associated with hospitalization-related functional decline, defined as a decline of 5 or more points on the Barthel Index at discharge[30]. Based on the results of the present study, preoperative physical activity through walking was associated with postoperative physical activity, and it was thought that the preoperative step count was related to FIM at discharge. Furthermore, Shimoda et al. reported that muscle mass decreases by 4.8% after esophageal surgery[31], and inflammation caused by invasion such as surgery causes metabolic changes such as protein breakdown in skeletal muscle[32]. Therefore, grip strength and knee extension muscle strength are affected by surgery. In other words, functional aspects such as grip strength and knee extension muscle strength were affected by surgery and were not considered to be related to preoperative physical activity. However, a relationship was observed between preoperative step count and 6MWD at discharge. Walking is used for 6MWD, and physical activity through walking before surgery improves physical activity through walking after surgery, as with FIM at discharge. Thus, it appears that the present results were obtained because the performance aspect of walking was maintained throughout this study. Regarding preoperative METs, no correlations were observed between all preoperative and postoperative items. The METs value in this study was the total score for various activities. On the other hand, the preoperative step count is related to preoperative ADLs, postoperative physical activity, and ADLs. This suggests that preoperative physical activity needs to be intense.

A limitation of this study is that the preoperative METs assessed various activities other than walking, but it has not been possible to verify the type of activity or intensity. Furthermore, it has not been possible to verify whether the preoperative step counts are measured by walking or other activities, and it is necessary to verify this together with METs. Furthermore, Hogenbirk et al.[33] reported that postoperative nutritional intake was associated with postoperative muscle mass loss, but this study did not examine postoperative nutritional status. Additionally, this was a single-center study, and the medical conditions, risk of bias, and sample size are different from those of multicenter studies. These results are from one institution and may not apply to all patients.

As for preoperative physical activity for esophageal cancer, the number of steps was associated with age and preoperative nutritional status and ADLs, physical activity after 7 days postoperatively, and exercise capacity and ADLs at discharge. Therefore, improving nutritional status and increasing physical activity through walking before surgery is thought to contribute to increasing the chances of postoperative mobilization and maintaining exercise tolerance and ADLs at the time of discharge. In addition, the step count and METs were used as indicators of preoperative physical activity, and the results were different for each of these measures. This suggests that preoperative physical activity may require increased intensity, but this issue requires further investigation.

Conflict of interest

There are no conflicts of interest to disclose.

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