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Effect of Perioperative Physical Activity on Skeletal Muscle Loss 6 Months After Esophageal Cancer Surgery

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Abstract. *Background/Aim: Sarcopenia contributes to a poor prognosis in patients with esophageal cancer; thus, any clinical support that prevents loss of skeletal muscle mass preoperatively and postoperatively should be actively investigated. This study aimed to evaluate physical activity during the perioperative period and its impact on postoperative skeletal muscle mass. Patients and Methods: Sixty-two patients who underwent esophagostomy at the Hamamatsu University School of Medicine between 2019 and 2023 were evaluated. The physical activity (measured by the step count) of patients scheduled for esophagectomy was assessed preoperatively using a fitness tracker. The percentage change in skeletal muscle mass index (SMI) was calculated preoperatively and 6 months postoperatively. Factors associated with decreased SMI 6 months after esophagectomy were analyzed using multivariate analysis. Results: The median decrease in SMI was –6.2%. Multivariate analysis revealed that factors associated with the reduction of SMI were age >69 years [odds ratio (OR)=7.21, 95% confidence interval (CI)=1.36-38.19, p=0.020], preoperative step count <7,800 steps/day (OR=5.17, 95% CI=1.38-19.33, p=0.015), and postoperative step count <2,400 steps/day (OR=3.55, 95% CI=1.01-12.45, p=0.048). Conclusion: A low perioperative step count and older age were significant risk factors for skeletal muscle loss in patients with esophageal cancer undergoing surgery. For patients with a low number of steps in the perioperative period or for older patients, interventions to increase the number of steps may prevent skeletal muscle loss.*

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Despite advances in minimally invasive surgery, esophageal cancer remains highly invasive with a high rate of postoperative complications (1, 2). Sarcopenia is a risk factor for postoperative complications, which underlines the importance of preventative measures before surgery (3). Sarcopenia is a condition characterized by reduced muscle strength and physical capacity due to loss of muscle volume. Sarcopenia is classified as primary sarcopenia when related to aging and as secondary sarcopenia when related to low activity, malnutrition, and disease (4). Low muscle mass may increase vulnerability to malnutrition, endocrine changes, muscle disuse, and low-grade systemic inflammation, and poor preoperative nutritional status affects prognosis (5). In addition, sarcopenia predicts chemotherapy toxicity and has an impact on prognosis (6). In contrast, recent studies have reported that patients undergoing esophagectomy have decreased skeletal muscle mass after surgery and an increased prevalence of sarcopenia in the long term (7-9). Therefore, interventions that prevent long-term postoperative skeletal muscle loss are urgently needed.

The Hamamatsu Perioperative Care Team (HOPE) intervenes with patients undergoing esophagectomy at the Department of Surgery, at Hamamatsu University School of Medicine. HOPE assesses the physical function and nutritional status of the patient and provides individualized care according to the patient's current condition. Prior to surgery, the patient is instructed by the physiotherapist to perform aerobic exercises, such as walking, and perform resistance exercise every day. After surgery, the patient is expected to walk on the following day (10). Furthermore, eligible patients should participate actively in preoperative rehabilitation using a treatment diary and fitness tracker (11). Esophagectomy is a highly invasive surgery that reduces postoperative physical activity levels (7).

Therefore, we focused on the mean number of steps as an indicator of perioperative activity levels to determine whether it influenced changes in skeletal muscle after esophagectomy.

Patients and Methods

Patients. Of the 195 patients scheduled for esophagectomy between March 2019 and March 2023 at the Department of Surgery of the Hamamatsu University School of Medicine, 81 patients who provided consent to wear a fitness tracker were included. This study was approved by the Ethics Committee of the Hamamatsu University School of Medicine. All study procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 1964 Helsinki Declaration and later versions. Informed consent was obtained from all patients.

Measurement of skeletal muscle loss. Skeletal muscle mass was assessed based on body composition, which was routinely measured. Body composition was measured using a direct-segment multifrequency bioelectrical impedance analyzer (DSM-BIA; InBody S10, Tokyo, Japan). Changes in skeletal muscle loss from the preoperative assessment to the 6-month postoperative follow-up were analyzed using changes in SMI. The calculation of percentage change was as follows: (postoperative SMI–preoperative SMI)/ preoperative SMI×100.

Assessment of physical activity. Physical activity was measured as the number of steps measured using a wristband fitness tracker. The Fitbit Alta HR or Fitbit Inspire HR (Fitbit, San Francisco, CA, USA) was used. The data obtained from the fitness trackers were considered valid when worn for at least 12 h/day for 3 consecutive days (12). We used data from preoperative 2 weeks and postoperative week 3 (15-21 days postoperatively) before discharge.

Analyzed parameters. Skeletal muscle loss was analyzed 6 months after esophagectomy. For this analysis, the median SMI reduction rate was used as the cutoff value to divide patients into two groups: the SMI mild-loss group and the SMI severe-loss group. Preoperative (age, sex, stage, blood test, and risk of malnutrition) and postoperative factors (postoperative complications and energy intake at discharge) related to the reduction of SMI 6 months after esophagectomy were examined. The risk of malnutrition was assessed using the Mini Nutritional Assessment—Short Form (MNA-SF) (13) for participants aged ≥65 years and the Malnutrition Universal Screening Tool (MUST) (14) for those aged <65 years. Individuals with an MNA-SF score ≤11 and a MUST score ≥1 were considered at risk. Postoperative complications were assessed using the Clavien–Dindo classification (15). The average energy intake and the ratio of nutritional requirements (NRs) of energy intake for meals, oral nutritional supplementation (ONS), and enteral nutrition (EN) were calculated 3 days before discharge. NR was calculated as the basal energy expenditure (BEE)×1.3. The BEE was calculated using the Harris–Benedict equation (16).

Statistical analyses. Continuous variables were checked for normality using histograms and normal Q–Q plots. Normally distributed variables are expressed as the mean±standard deviation. Non-normally distributed variables were expressed as medians [interquartile ranges]. Nominal variables were expressed as the number of subjects (percentage). Comparisons between the two groups divided by the rate of SMI reduction were performed using Student's *t*-test or Mann-Whitney *U*-test for continuous variables and Chi-squared test or Fisher's direct probability test for nominal variables. Weight, body mass index (BMI), skeletal muscle mass index (SMI), prognostic nutritional index (PNI), albumin levels, and transthyretin levels were compared before and after surgery using the paired *t*-test to confirm postoperative changes. Statistical significance was defined as a two-tailed *p*-value <0.05. To identify factors related to reduction in skeletal muscle mass 6 months after esophagectomy, a logistic regression analysis was performed. The cutoff values for continuous variables were as follows: BMI and respiratory function were standard values, and the PNI, albumin level, and transthyretin level were considered mean values. The cutoff values for age, preoperative and postoperative step counts, and energy intake ratio at discharge were calculated from receiver operating characteristic (ROC) curves. The preoperative step count of 7,779 steps/day was set to 7,800 steps/day, and the postoperative step count of 2,376 steps/day was set to 2,400 steps/day. The rate of food and ONS intake relative NRs at discharge was 57.6%, EN intake was 33.9%, and total energy intake was 85.1%. Multivariate analysis included variables with $p<0.05$ in univariate analysis. The area under the curve (AUC) were calculated from the ROC curves of the factors extracted in the multivariate analysis. The correlations between the preoperative and postoperative steps and the SMI reduction rate and risk factors 6 months after surgery were measured using Pearson product-moment correlation coefficient. All analyses were performed using IBM SPSS statistics version 29.0 for Mac (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics. Of the 81 patients, 19 were excluded for the following reasons: 2 patients did not undergo surgery; 2 patients refused to wear a tracker; 3 patients had two-stage surgery; 6 patients did not have body composition measurement; 3 patients changed hospitals; 3 patients died. The final analysis included 62 patients, of whom 51 were male and 11 were female (Figure 1). The clinical classification of cancer progression was stage 0 in 1 case, stage 1 in 21 cases, stage 2 in 14 cases, stage 3 in 23 cases, and stage 4 in 3 cases. Twenty-eight patients (45.2%) received preoperative chemotherapy. The surgical procedure was thoracoscopic esophagectomy in 49 patients (79.0%), which included robot-assisted surgery. Overall, postoperative complications of Clavien–Dindo grade II or higher occurred in 12 patients (19.4%), and grade III or higher complications occurred in 7 patients (11.3%). The incidence of postoperative pneumonia was 1.6% (1 case), and the incidence

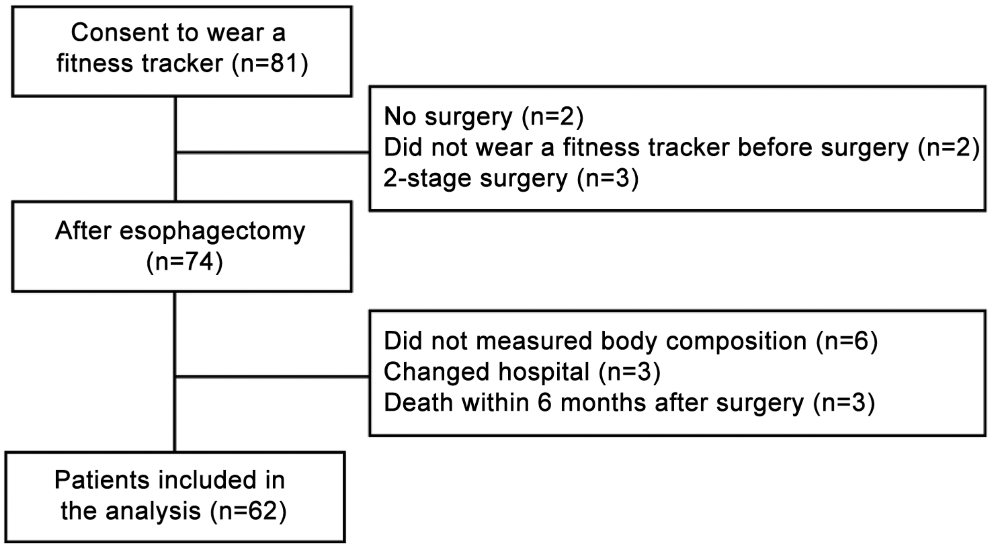

Figure 1. *Flowchart of study participants.*

of anastomotic leakage was 12.9% (8 cases). The mean numbers of steps/day before and after surgery were 8,160 and 3,335 steps/day, respectively. Postoperative step count was significantly lower in the SMI severe loss group (4,163 *vs.* 2,536 steps/day, p=0.022) (Table I).

Changes in body composition and nutritional indicators based on blood tests before and after surgery are shown in Table II. The postoperative change in weight compared with the preoperative weight was –10.1%±6.3% (p<0.001). The perioperative change in BMI was –10.3%±5.5% (p<0.001). Preoperative and postoperative SMIs were 7.2±1.1 and 6.8±1.0 kg/m2, respectively, and the perioperative change rate of SMI was –6.2%±6.7%. There was no difference in PNI and albumin levels, but transthyretin levels decreased significantly after surgery (27.3 *vs.* 22.4 g/dl, p<0.001).

Factors related to SMI reduction 6 months after esophagectomy. Multivariate analysis revealed that factors associated with SMI reduction 6 months after surgery were age >69 years (OR=7.21, 95% CI=1.36-38.19, p=0.020), preoperative step count <7,800 steps/day (OR=5.17, 95% CI=1.38-19.33, p=0.015), and postoperative step count <2,400 steps/day (OR=3.55, 95% CI=1.01-12.45, p=0.048) (Table III). The AUC from ROC curves obtained for each factor assesses the ability to predict the SMI reduction, and the following AUCs were obtained: age, 0.65 (95% CI=0.51-0.79); preoperative step count, 0.61 (95% CI=0.46-0.75); postoperative step count, 0.69 (95% CI=0.55-0.82) (Table IV).

The postoperative number of steps was significantly correlated with the preoperative number of steps (r=0.533, 95% CI=0.32-0.69, p<0.001) (Figure 2).

Discussion

The main finding of the study was that age and perioperative step count were independent predictors of skeletal muscle loss 6 months after esophagectomy. To our knowledge, this is the first report evaluating the relationship between age and perioperative step count and long-term skeletal muscle loss after esophagectomy. Furthermore, we showed a correlation between the number of preoperative and postoperative steps. This suggests the importance of maintaining or increasing activity levels in anticipation of the postoperative period in patients with low preoperative activity levels.

Esophagectomy is a highly invasive procedure that increases the likelihood of skeletal muscle loss associated with postoperative hypoactivity compared to other gastrointestinal cancer surgeries. As skeletal muscle loss is associated with prognosis in patients with esophageal cancer, it is important to identify the risk of skeletal muscle loss and to prevent it (17). Previous reports have identified factors associated with loss of skeletal muscle in postoperative patients with esophageal cancer, including preoperative BMI, postoperative grip strength, tube feeding at discharge (8), percentage change in quadriceps muscle strength 1 month after surgery (9), and activity level immediately after discharge (7). In our study, the median rate of reduction of SMI at 6 months postoperatively was 6.2%, which is a new finding suggesting that the perioperative step count is an influential factor. With respect to physical activity and skeletal muscle mass, increasing the number of daily steps may decrease the risk of developing sarcopenia in older patients (18). Therefore, walking is considered an important factor for the prevention of skeletal muscle loss. Furthermore, in this

Table I. *Patient characteristics*.

	Total (n=62)	SMI mild loss (n=30)	SMI severe loss (n=32)	*p*-Value
Age (years)	65±9.1	62±7.6	67±10.1	0.061
Male/female	51/11	25/5	26/6	0.548
ASA score				
1/2/3/4	4/56/1/1	2/28/0/0	2/28/1/1	0.585
Clinical stage				
0/1/2/3/4	1/21/14/23/3	1/10/8/8/3	0/11/6/15/0	0.171
Preoperative chemotherapy	28 (45.2)	13 (43.3)	15 (46.9)	0.490
Weight (kg)	60.2±10.8	61.2±10.1	59.2±11.4	0.465
BMI (kg/m^2)	22.1±2.7	21.9±2.6	22.3±2.8	0.585
SMI (kg/m^2)	7.2±1.1	7.2±1.0	7.2±1.2	0.939
Risk of malnutrition	39 (62.9)	20 (66.7)	19 (59.4)	0.371
PNI	48.6±4.3	48.8±4.0	48.4±4.6	0.701
Albumin level (g/dl)	4.1±0.4	4.1±0.4	4.1±0.4	0.749
Transthyretin level (g/dl)	27.3±5.4	27.9±5.8	26.9±5.2	0.504
Respiratory function				
%VC (%)	104.8±14.3	106.5±14.9	103.2±14.1	0.379
FEV1.0% (%)	74.0±7.7	74.1±7.0	74.0±8.6	0.956
Preoperative steps (steps/day)	8,160±3,044	8,851±3,257	7,511±2,672	0.088
Surgical procedure				0.553
Open esophagectomy	13 (21.0)	6 (20.0)	7 (21.9)	
Thoracoscopic esophagectomy	49 (79.0)	24 (80.0)	25 (78.1)	
Complications				
CD grade II or higher	12 (19.4)	5 (16.7)	7 (21.9)	0.423
CD grade III or higher	7 (11.3)	4 (13.3)	3 (9.4)	0.463
Pneumoniaa	1 (1.6)	0	1 (3.1)	0.516
Anastomotic leakage[a]	8 (12.9)	4 (13.3)	4 (12.5)	0.609
Postoperative steps (steps/day)[b]	3,335±2,725	4,163±3,325	2,536±1,622	0.022
Postoperative hospital stay (days)	22 [19-26]	21 [19-26]	23 [20-27]	0.177
Oral energy intake (food+ONS)[c] (%)	48 [33-64]	50.7 [36.4-67.6]	46.1 [32.0-58.5]	0.254
EN intake[c] (%)	33.4 [27.4-37.7]	31.7 [23.2-37.3]	35.4 [29.0-38.2]	0.467
Total energy intake[c] (%)	83.8 [70.0-94.8]	82.5 [71.2-96.7]	85.3 [67.6-93.0]	0.767
Postoperative chemotherapy within 6 months	26 (41.9)	14 (46.7)	12 (37.5)	0.318

Variables are expressed as mean±standard deviation, number of patients (percentages), and median [interquartile range: 25th percentile to 75th percentile]. ASA, American Society of Anesthesiologists physical status; BMI, body mass index; SMI, skeletal muscle mass index; PNI, prognostic nutritional index; %VC, percentage of vital capacity; FEV1.0%, forced expiratory volume % in 1 s; CD, Clavien-Dindo classification; ONS, oral nutritional supplementation; EN, enteral nutrition. [a]CD class II or higher. [b]Values at 3 weeks after surgery. [c]Ratio to the nutritional requirements of energy intake during the 3 days before discharge.

study, the preoperative step count was significantly correlated with the postoperative step count. Similar to previous studies, our results suggest that the preoperative step count may be a predictive indicator of the risk of postoperative hypoactivity (19). Previous studies have shown that preoperative activity levels can predict postoperative complications and delirium (20, 21). In older patients, the number of steps and maximum oxygen consumption (VO_{2Max}) measured using a wearable device before surgery correlate with the 6- Minute Walk Test and Clinical Frailty Scale, suggesting that they may be indicators of mobility and frailty (22). Collectively, the preoperative step count may be more useful in identifying patients for intervention.

Although the importance of combined exercise therapy and nutritional intervention for sarcopenia has been suggested (23), the result of this study may provide additional important information. Although active intervention to prevent sarcopenia is important, the correlation between preoperative and postoperative step counts suggests the importance of intervention in overall daily living throughout the perioperative period for patients with low activity levels. Identifying the factors that contribute to the decline in activity levels and interventions to address these factors will help improve activity levels. The number of steps can also be monitored using a smartphone, which is a convenient indicator of activity levels and is useful for patient guidance (24). Furthermore, based on the present results, daily support to increase physical activity in older patients should also be considered.

Compared to other studies on preoperative cancer patients, the mean number of preoperative steps of 8,160 steps/day

Table II. *Comparison of variables before and after surgery.*

	Preoperative	Postoperative[a]	Perioperative change (%)	*p*-Value
Weight (kg)	60.2±10.8	54.0±9.4	–10.1±6.3	<0.001
BMI (kg/m^2)	22.1±2.7	19.8±2.2	–10.3±5.5	<0.001
SMI (kg/m^2)	7.2±1.1	6.8±1.0	–6.2±6.7	<0.001
PNI	48.6±4.3	49.4±5.0		0.240
Albumin level (g/dl)	4.1±0.4	4.1± 0.3		0.879
Transthyretin level (g/dl)	27.3±5.4	22.3±4.2		<0.001

Variables are expressed as mean±standard deviation. BMI, Body mass index; SMI, skeletal muscle mass index; PNI, prognostic nutritional index. [a]Values at 6 months after surgery.

Table III. *Multivariate logistic regression analysis of risk factors for SMI reduction at 6 months after surgery.*

	Univariate logistic regression			Multiple logistic regression		
	Odds ratio	95% CI	*p*-Value	Odds ratio	95% CI	*p*-Value
Preoperative factors						
Age >69 years	7.00	1.76-27.89	0.006	7.21	1.36-38.19	0.020
Sex (male *vs*. female)	1.15	0.31-4.27	0.830			
Clinical stage (0, 1, 2 *vs*. 3, 4)	1.52	0.55-4.21	0.417			
Preoperative chemotherapy (present *vs*. absent)	1.15	0.42-3.14	0.779			
BMI <22 kg/m^2	1.02	0.37-2.78	0.974			
SMI	1.02	0.64-1.62	0.938			
Risk of malnutrition (present *vs*. absent)	0.73	0.26-2.06	0.553			
Albumin level <4.0 g/dL	0.73	0.41-1.46	0.425			
Transthyretin level <22.5 g/dl	0.71	0.34-1.48	0.356			
PNI <49.0	0.75	0.36-1.59	0.451			
%VC <80	0.97	0.13-7.33	0.973			
FEV1.0% <70	1.31	0.43-4.00	0.633			
Preoperative steps <7,800 steps/day	3.41	1.19-9.77	0.022	5.17	1.38-19.33	0.015
Postoperative factors						
Complication CD grade II or higher	1.40	0.39-5.00	0.605			
Complication CD grade III or higher	0.72	0.14-3.30	0.624			
Postoperative hospital stay >22 days	1.70	0.62-4.66	0.302			
Oral energy intake (food+ONS)[a] <58%	2.63	0.90-7.69	0.078			
EN intake[a] >34%	2.27	0.81-6.34	0.119			
Total energy intake[a] <85%	0.59	0.22-1.61	0.302			
Postoperative steps <2,400 steps/day	5.43	1.76-16.79	0.003	3.55	1.01-12.45	0.048
Postoperative chemotherapy within 6 months (present *vs*. absent)	0.69	0.25-1.89	0.466			

CI, Confidence interval; BMI, body mass index; SMI, skeletal muscle mass index; PNI, prognostic nutritional index; %VC, percentage of vital capacity; FEV1.0%, forced expiratory volume in 1 s; CD, Clavien-Dindo classification; ONS, oral nutrition supplementation; EN, enteral nutrition. [a]Ratio to the nutritional requirements of energy intake during the 3 days before discharge.

was relatively high (19, 25) and comparable to that of healthy people of the same age (26). It is possible that the participants in this study took more steps because they were encouraged to remain active, in addition to the fact that the use of a fitness tracker is known to increase the number of steps (27). In contrast, the mean number of steps at postoperative week 3 was 3,335 steps/day. It is expected to take weeks to months for the postoperative gait to return to

Table IV. *Cutoff value, AUC, and 95% CI in SMI reduction at 6 months after surgery.*

	Cutoff value	AUC	95% CI	*p*-Value
Age	69	0.65	0.51-0.79	0.041
Preoperative steps	7,779	0.61	0.46-0.75	0.152
Postoperative steps	2,376	0.69	0.55-0.82	0.008

AUC, Area under the curve; CI, confidence interval.

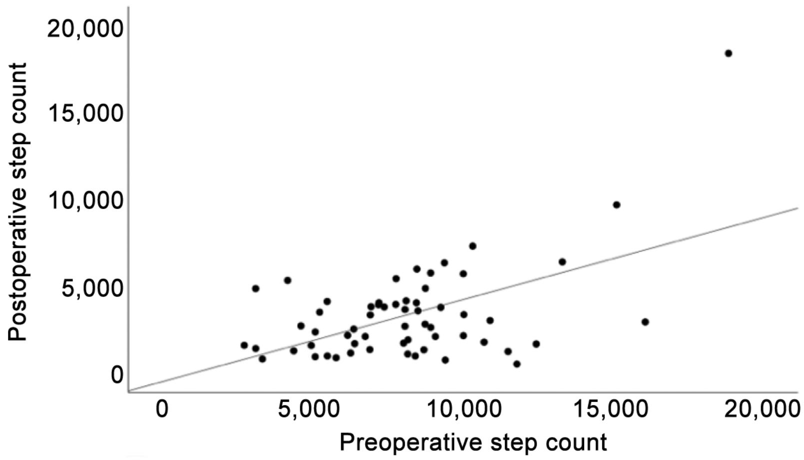

Figure 2. *Correlation between preoperative and postoperative step count.*

baseline (25). Furthermore, the degree of recovery varies depending on the individual patient; therefore, it is difficult to use the cutoff values of this study or the number of steps taken by healthy older adults as a guide. Furthermore, a study of patients undergoing gastrointestinal cancer surgery found that a targeted step count intervention increased fatigue (28). Therefore, it is important to evaluate both postoperative and perioperative step counts, and to provide appropriate intervention and support to patients (25).

Esophageal cancer in Japanese tends to appear in their 60s to 70s, accounting for approximately 70% of all patients (29). In this study, age >69 was one of the risk factors associated with a decrease in SMI at 6 months postoperatively. A previous study investigating risk factors for skeletal muscle loss during neoadjuvant therapy for esophageal cancer found that age ≥70 was one of them (30). Furthermore, in a study of esophageal cancer patients who underwent surgery, the enhanced recovery after surgery program (ERAS) showed better postoperative body composition the patients who received the old program, but compliance with the ERAS program was lower in patients age ≥70 (31). Collectively, it is necessary to consider effective ways to support older patients with esophageal cancer to prevent skeletal muscle loss. Future research directions in this area should examine the effectiveness of interventions based on the number of steps taken in daily life, considering the physical condition and energy intake of postoperative patients with esophageal cancer.

Study limitations. First, only a limited number of cases from a single Institution were analyzed. Furthermore, the participants in the study were patients who agreed to wear a fitness tracker, which may not have been universal, because they may have been more motivated to be active. Second, this study only assessed the reduction in SMI and not physical performance. Therefore, its association with sarcopenia must be examined.

Conclusion

This study confirmed that older age and low perioperative step count are significant risk factors for postoperative loss of skeletal muscle in patients with esophageal cancer undergoing surgery. For patients with a low number of steps in the perioperative period or those who are older, preoperative intervention to increase the number of steps may prevent skeletal muscle loss.

Conflicts of Interest

All Authors declare that they have no conflicts of interest.

Authors' Contributions

Study conception and design: JH and YH. Provision of study materials or patients: SK, YH, HK, and HT. Collection and assembly of data: JH, HY, KM, SK, and YM. Final approval of manuscript: All Authors.

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