Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Analysis of the associated factors for severe weight loss after minimally invasive McKeown esophagectomy

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Keywords
Esophageal neoplasm; esophagectomy; risk factor; weight loss.

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Received: 12 October 2018;
Accepted: 14 November 2018.

doi: 10.1111/1759-7714.12934

Thoracic Cancer **10** (2019) 209–218

Abstract

Background: This study investigated the risk factors for severe weight loss (SWL) within one year after minimally invasive McKeown esophagectomy.

Methods: Esophageal cancer patients who underwent McKeown esophagectomy between January and July 2017 were prospectively enrolled. Preoperative body weight (PBW) was chosen as the initial body weight.

Results: Forty-four patients were enrolled and successfully followed up for one year. Median weight loss was 7.4% (quartile: 5.3–8.1%) and 12.6% (quartile: 8.8–17.7%) four weeks and one year after surgery, respectively. Accelerated weight loss occurred during the first two weeks after discharge, with median weight loss of 5.6% (quartile: 4.2–7.1%). Multivariable analysis showed that age ≥ 70 years (odds ratio [OR] 7.65; $P = 0.030$), preoperative sarcopenia (OR 7.18; $P = 0.030$), the first surgery in the daily schedule (OR 6.87; $P = 0.032$) and vocal cord paralysis (OR 12.30; $P = 0.046$) were independent risk factors for short-term (4 weeks) SWL (> 7.5% PBW), while an American Society of Anesthesiologists score of 3–4 (OR 6.58; $P = 0.047$), a high fat-free mass (OR 21.91; $P = 0.003$), and vocal cord paralysis (OR 25.83; $P = 0.017$) were independent risk factors for long-term (1 year) SWL (> 13.0% PBW) after esophagectomy. Postoperative symptoms of insomnia, appetite loss, dysphagia, eating difficulties, and taste issues were also related to SWL.

Conclusions: In esophageal cancer patients who have undergone esophagectomy, the first two weeks after hospital discharge is a key period for nutrition intervention. Patients with associated factors for SWL require postoperative nutrition support.

Introduction

Esophageal cancer is the 11th most common cancer and the sixth most common cause of perioperative mortality worldwide.[1] Esophagectomy or neoadjuvant therapy followed by esophagectomy is the critical therapy for this malignant tumor.[2] Postoperative weight loss is a common problem in patients with esophageal cancer, and severe weight loss (SWL) is closely related to poor prognosis.[3,4] However, the degrees of postoperative body weight changes and the risk factors for SWL have not been identified.[5,6] The purpose of this study was to prospectively observe body weight changes in patients who underwent minimally invasive McKeown esophagectomy (McKeown-MIE) to explore the regularity of body weight changes and to analyze the risk factors leading to SWL.

Methods

Study design and patients

Patients who underwent McKeown-MIE as initial treatment from January to July 2017 at the Department of

Thoracic Surgery, Affiliated Cancer Hospital of Zhengzhou University were prospectively included. The inclusion criteria were: (i) age 18–80 years, (ii) preoperative diagnosis of esophageal cancer, and (iii) good cardiopulmonary function that was evaluated to tolerate surgery. The exclusion criteria were: (i) a preoperative examination that showed that the tumor had invaded into surrounding tissues, lymph nodes, and important organ metastases; (ii) esophagectomy after neoadjuvant therapy; and (iii) a history of previous gastrointestinal malignancies, rheumatic immune disease, or inflammatory bowel disease.

This study met the ethical standards of the Affiliated Cancer Hospital of Zhengzhou University Ethics Committee. All patients signed informed consent prior to their inclusion in the study.

Data collection

Patients' body composition was assessed at 7:00 a.m. on the operation day using multifrequency bioelectrical impedance with eight tactile electrodes (BCA-IB Body Component Analyzer, Tsinghua Tongfang Co. Ltd., Beijing, China). Various parameters, including the fat-free mass (FFM), skeletal muscle, and fat mass were automatically measured. Preoperative sarcopenia (depletion of skeletal muscle mass) was diagnosed as skeletal muscle below the normal range of the Chinese population provided by the BCA-IB Body Component Analyzer.[7] Body mass index (BMI) was calculated as the weight in kilograms divided by the height in square meters (kg/m^2), and was classified according to the Asian-specific BMI cut-off.[8] Preoperative performance status was assessed using Eastern Cooperative Oncology Group performance status (ECOG-PS) and Karnofsky Performance Status (KPS).[9,10]

For clinical data collection, the included patients were staged before and after surgery according to the eighth edition American Joint Committee on Cancer/Union for International Cancer Control Tumor Node Metastasis (TNM) Classification.[11,12] Preoperative clinical staging was based on esophagography, endoscopy, endoscopic ultrasonography (EUS), and computed tomography (CT) of the chest and upper abdomen. A biopsy of the cervical lymph nodes and positron emission tomography were used to determine the clinical stage if needed. Postoperative complications were defined according to the international consensus on the standardization of data collection for complications associated with esophagectomy produced by the Esophagectomy Complications Consensus Group, and graded according to the Clavien–Dindo classification.[13,14]

To measure and follow-up body weight, weight was measured in the morning after defecation on an empty stomach with a single layer of clothes. The figures were accurate to 0.1 kg, and the average of three consecutive measurements was used as the final measurement. The preoperative body weight (PBW) was measured on the morning of the operation day. Patients' body weight was measured every three to four days over four weeks, every week from 5 to 12 weeks, and every two weeks from 13 to 56 weeks after surgery. Follow-up was arranged by telephone, and details were explained to patients ahead of time to ensure the accuracy of weight measurement. Data were collected by email.

Surgery and recovery

All patients underwent McKeown-MIE with a two-field lymph node dissection, and anastomosis was performed to sew up the gastric conduit to the distal esophagus, as previously described.[15,16] All operations were performed by one surgical team led by one author. The "non-tube no fasting" fast-track program was the first choice for all patients, except when symptoms of aspiration or the appearance of serious complications arose, at which time oral feeding was delayed or ceased.[15,17] Normally the nutrition provided by intravenous approach decreases with the increase in oral feeding, and is removed on the fourth day after surgery. The need for adjuvant therapy after surgery is determined by the pathology stage and the patients' aspiration and nutrition status.

Quality of life

The European Organization for Research and Treatment of Cancer questionnaires C30 and OES18 were used to assess quality of life (QOL) at baseline (1 week before surgery) and 2, 4, 8, 12, and 24 weeks after surgery. Questionnaire scales related to intake and body weight recovery were analyzed to investigate the association between QOL and postoperative weight loss. Baseline data were collected in the hospital and follow-up assessments were arranged by telephone and performed by mail, with one telephone reminder if required.

Statistical analysis

The categorical data are presented as the frequency (percentage), and the continuous data are presented as the mean $\pm$ standard deviation or the medians and interquartile ranges according to the results of the Shapiro–Wilk test. QOL data are presented as mean $\pm$ standard deviation. Comparisons between the groups were performed using the *t*-test for independent samples in cases of normal data distribution and the Mann–Whitney *U* test in cases of non-normal data distribution. Univariate and multivariate logistic regression models were used to analyze the risk factors. The continuous variables were grouped according to the mean, median, and practical significance to be included in risk

factor analysis. A two-tailed P value of < 0.05 was considered statistically significant. All analyses were conducted using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 45 patients met the study criteria during the study period. All of the patients were included in the study after signing informed consent, and the baseline data collection rate was 100%. One patient dropped out of the study three weeks after surgery, and 44 patients were followed up for one year. No perioperative or follow-up death occurred and no tumor recurrence or metastasis.

Table 1 Basic patient characteristics and clinical data

Variables	Values
Demographic data, N (%)	
Age (years), mean ± SD	65.7 ± 7.7
Gender (male)	26 (59.1)
Brinkman index† (≥ 100)	18 (40.9)
Alcohol index‡ (≥ 2000)	7 (15.9)
Preoperative morbidity, N (%)	
Diabetes	3 (6.8)
Cardiovascular disease	11 (25.0)
COPD	4 (9.1)
Cerebral vascular disease	6 (13.6)
ASA score 3–4	19 (43.2)
ECOG PS score > 1 point	11 (25)
KPS score < 90%	13 (29.5)
Preoperative nutrition, mean ± SD	
Body weight (kg)	66.1 ± 7.8 (male); 54.9 ± 5.7 (female)
FFM (kg)	49.9 ± 6.2 (male); 37.7 ± 3.4 (female)
Fat mass (kg)	16.3 ± 4.2 (male); 17.3 ± 3.5 (female)
Weight loss in last 3 months (%)	4.3 ± 0.5
BMI (kg/m^2)	23.1 ± 2.3
Preoperative sarcopenia, N (%)	18 (40.9)
Tumor characteristics, N (%)	
Location (upper/middle /lower)	2 (4.5)/ 29 (65.9)/13 (29.5)
cT (T0-1/T2-3)	19 (43.2)/25 (56.8)
cN (N0/ N1)	34 (77.3)/10 (22.7)
pTNM (0–I/II–III)	19 (43.2)/25 (56.8)
Histological type (SCC/AC)	43 (97.7)/1 (2.3)
Differentiation (well/ moderately/poorly)	9 (20.5)/ 21 (47.7)/14 (31.8)
Tumor length (mm), mean ± SD	47.5 ± 19.3
Adjuvant therapy, N (%)	1 (2.3%)§

†Brinkman index = daily count of cigarettes × smoking years. ‡Alcohol index = daily alcohol consumption (g) × drinking years. §One patient underwent postoperative chemotherapy. AC, adenocarcinoma; ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ECOG PS, Eastern Cooperative Oncology Group performance status; FFM, fat-free mass; KPS, Karnofsky Performance Status; pTNM, pathological tumor node metastasis; SCC, squamous cell carcinoma; SD, standard deviation.

Data characteristics

The patient characteristics are shown in Table 1. There were 26 (59.1%) men and 18 (40.9%) women at an average age of 65.7 ± 7.7. Squamous cell carcinoma (SCC) dominated the pathological types, with 43 (97.7%) patients. The perioperative parameters and postoperative complications are shown in Table 2. In total, 31 (70.5%) patients successfully completed the fast-track program, oral feeding was delayed to the fourth day after surgery in 9 (20.5%) patients because of aspiration, 3 (6.8%) patients did not complete the fast-track program and underwent gastrointestinal decompression because of severe stomach distention, and 1 (2.3%) patient returned to the intensive care unit and oral feeding was stopped because of acute respiratory distress syndrome. Among the 9 (20.5%) patients with symptoms of aspiration, 7 (15.9%) patients developed vocal cord paralysis (VCP) because of the operation, 1 (2.3%) patient developed VCP because of

Table 2 Perioperative parameters and postoperative complications

Variables	Values
Operative parameters	
Operation order (first/others), N (%)	21 (47.7)/23 (52.3)
Operative time (minutes), mean ± SD	185.0 ± 38.0
Blood loss (mL), mean ± SD	97.5 ± 30.2
Curability (R0/R1-2), N (%)	44 (100)/0 (0)
Postoperative complications, N (%)	
Cardiac dysrhythmia	5 (11.4)
Pneumonia	4 (9.1)
Pleural effusion	4 (9.1)
ARDS	1 (2.3)
VCP	7 (15.9)
Wound infection	2 (4.5)
Pulmonary embolus	1 (2.3)
Anastomotic leakage	0 (0)
Other complications	2 (4.5)
Overall complications†	13 (29.5)
Recurrent need of ICU treatment	2 (4.5)
In-hospital mortality	0 (0)
Clavien–Dindo classification (Grade 0–2/3–4)	9 (20.5)/4 (9.1)
Postoperative recovery	
Fast track program, N (%)	31 (70.5)
Length of postoperative stay, mean ± SD	9.0 ± 3.2
Perioperative serum parameters, mean ± SD	
Preoperative serum prealbumin (mg/L)	203.3 ± 63.6
Preoperative serum albumin (g/L)	43.7 ± 3.9
POD1 serum prealbumin (mg/L)	148.0 ± 33.2
POD1 serum albumin (g/L)	33.2 ± 3.8
POD7 serum prealbumin (mg/L)‡	109.3 ± 27.2
POD7 serum albumin (g/L)‡	36.6 ± 3.8

†Defined as the presence of one or more of the complications listed above in a single patient. ‡Data was missing for three patients. ARDS, acute respiratory distress syndrome; ICU, intensive care unit; POD, postoperative day; SD, standard deviation; VCP, vocal cord paralysis.

recurrent nerve injury caused by preoperative cervical lymph node biopsy, and 1 (2.3%) patient developed VCP as a result of a previous recurrent nerve injury caused by thyroidectomy.

Weight changes

The preoperative average weight of the 44 patients was 61.5 ± 8.9 kg, and this value decreased to 55.1 ± 8.8 kg one year after surgery. Using the PBW as a reference, the changes in the body weight in each period after surgery are presented in Table 3. The median and quartile weight loss rates at one year were 12.6% (8.8–17.7%), and the maximum weight loss rate within the first year was 13% (9.5–17.7%). We also drew a line chart to describe patient's weekly body weight changes after surgery (Fig 1). We noticed that the patients' weight loss was concentrated within four weeks after surgery, while the change in body weight in the first week was minor. Considering that the length of the hospitalization was 9.0 ± 3.2 days, we speculated that the patients underwent accelerated weight loss in the short term after discharge. Subsequently, we analyzed the changes in body weight in and out of the hospital, with the discharge time as the observation point (Table 3). We observed that accelerated weight loss occurred in the first two weeks after discharge, with a weight loss rate of 5.6% (4.2–7.1%), contributing to 46.4% ± 16.7% of the maximum weight loss within one year after surgery.

Table 3 Patient' body weight changes after esophagectomy†

Time	Weight loss (%)‡ (median and quartile)	Contributing to 1-year MWL (%)§ (mean ± SD)
1st week AO	−0.2 (−0.7, 0)	2.6 ± 4.7
2nd week AO	−3.4 (−5.2, −2.4)	29.1 ± 13.4
3rd week AO	−2.2 (−3.2, −1.3)	17.5 ± 9.7
4th week AO	−0.6 (−1.4, −0.3)	7.0 ± 7.7
1–4 weeks AO	−7.4 (−8.1, −5.3)	56.3 ± 18.0
1–12 weeks AO	−9.8 (−11.8, −5.9)	68.9 ± 18.3
1–24 weeks AO	−10.6 (−14.1, −9.1)	81.0 ± 24.6
1 year AO	−12.6 (−17.7, −8.8)	100
In-hospital	−0.3 (−0.8, +0.1)	2.5 ± 5.7
1st week AD	−3.6 (−5.5, −2.5)	34.3 ± 15.9
2nd week AD	−1.3 (−2.6, −1.0)	14.7 ± 9.5
3rd week AD	−0.5 (−1.2, −0.3)	6.7 ± 7.9
4th week AD	−0.2 (−0.6, 0.0)	2.9 ± 4.4
1–2 weeks AD	−5.6 (−7.1, −4.2)	46.4 ± 16.7
1–4 weeks AD	−7.1 (−7.9, −5.4)	55.8 ± 17.8

†Preoperative body weight was chosen as initial body weight. ‡Negative values (−) mean weight loss; positive values (+) mean weight gain. §Calculated as the weight loss during the corresponding period divided by the maximum weight loss (MWL) within the first year after surgery; weight gain was noted as 0%. AD, after discharge; AO, after operation; SD, standard deviation.

Risk factors for short-term (4 weeks) severe weight loss after esophagectomy

The patients' average weight loss rate at four weeks after surgery was 7.6% ± 3.8%, with a median weight loss rate of 7.4% (quartile: 5.3–8.1%). Therefore, a weight loss rate > 7.5% was chosen as the criteria to recognize SWL at four weeks after surgery. Twenty (45.5%) patients were assigned to the SWL group and 24 (54.5%) to a normal weight loss (NWL) group. The outcomes of the univariate logistic regression models are presented in Table 4. Age ≥ 70 years (odds ratio [OR] 4.50; $P = 0.022$), ECOG PS > 1 (OR 9.00; $P = 0.011$), KPS < 90% (OR 5.73; $P = 0.022$), preoperative sarcopenia (OR 7.06; $P = 0.004$), a poorly differentiated tumor (OR 10.67; $P = 0.047$), the first surgery in the daily schedule (OR 3.71; $P = 0.040$), VCP (OR 15.33;

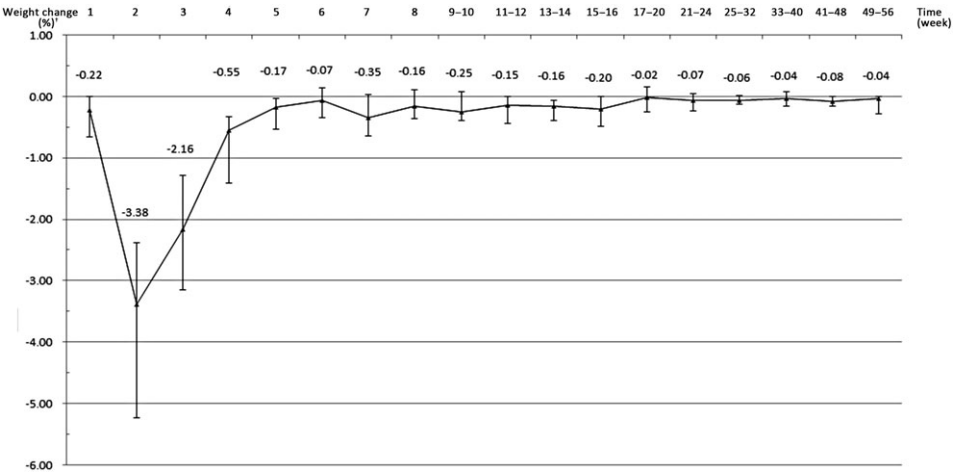

Figure 1 Line chart of patient's weekly body weight changes within a year after esophagectomy. Using the preoperative body weight as a reference, patient's body weight changes (%) per week during the first eight weeks and the average weekly weight changes (%) over the corresponding period are presented as the medians and interquartile ranges in the figure, while only values of the median are provided. † negative values (−) mean weight loss, positive values (+) mean weight gain.

Table 4 Outcomes of univariate analysis of the risk factors for SWL

	4W SWL (n = 20)†		1-year SWL (n = 21)‡	
Variables	OR (95% CI)	*P*	OR (95% CI)	*P*
Demographic data				
Age ≥ 70 years	4.50 (1.24–16.28)	0.022	1.71 (0.51–5.73)	0.389
Gender (male)	0.73 (0.22–2.45)	0.615	1.25 (0.37–4.17)	0.717
Brinkman index ≥ 100	0.43 (0.12–1.49)	0.183	0.80 (0.24–2.67)	0.717
Alcohol index ≥ 2000	0.42 (0.07–2.46)	0.338	0.79 (0.16–4.04)	0.779
Preoperative morbidity				
Diabetes	3(17): 0(22)*	0.300	0.53 (0.04–6.25)	0.610
Cardiovascular disease	2.49 (0.66–11.06)	0.170	2.38 (0.58–9.72)	0.229
COPD	4.06 (0.39–42.49)	0.242	3.67 (0.35–38.35)	0.278
Cerebral vascular disease	2.75 (0.45–16.90)	0.275	6(15): 0(23)*	0.020
ASA score 3–4	2.44 (0.72–8.31)	0.153	4.60 (1.28–16.58)	0.020
EOCG-PS score > 1 point	9.00 (1.65–49.00)	0.011	2.38 (0.58–9.72)	0.229
KPS score < 90%	5.73 (1.28–25.58)	0.022	0.18 (0.47–6.90)	0.391
Preoperative nutrition				
High body weight	1.40 (0.42–4.62)	0.581	3.72 (1.06–12.98)	0.040
High FFM§	1.71 (0.52–5.67)	0.379	7.08 (1.88–26.72)	0.004
High fat mass	0.82 (0.25–2.69)	0.741	1.43 (0.44–4.69)	0.555
Weight loss in last 3 months ≥ 5%	1.62 (0.46–5.68)	0.452	2.13 (0.60–7.57)	0.245
BMI ≥ 23 (kg/m^2)	0.87 (0.26–2.89)	0.824	2.18 (0.64–7.40)	0.211
Preoperative sarcopenia	7.06 (1.84–27.14)	0.004	2.51 (0.73–8.64)	0.143
Tumor characteristics				
Location (lower vs. upper/middle)	0.67 (0.18–2.50)	0.547	2.22 (0.59–8.34)	0.240
Differentiation				
Moderate (vs. well)	8.80 (0.93–83.35)	0.058	13.00 (1.36–124.30)	0.026
Poorly (vs. well)	10.67 (1.04–109.94)	0.047	8.00 (0.78–82.05)	0.080
pTNM				
Stage II (vs. 0–I)	1.03 (0.26–4.17)	0.966	1.03 (0.26–4.17)	0.966
Stage III (vs. 0–I)	1.65 (0.37–7.37)	0.512	2.41 (0.52–11.10)	0.260
Positive lymph nodes status	1.62 (0.44–5.96)	0.471	2.22 (0.59–8.34)	0.240
Tumor length ≥ 50 mm	0.79 (0.24–2.62)	0.697	0.97 (0.30–3.23)	0.967
Perioperative parameters				
The first operation (vs. others)	3.71 (1.06–12.98)	0.040	2.07 (0.62–6.91)	0.235
Operation time ≥ 190 minutes	1.71 (0.52–5.67)	0.379	2.07 (0.62–6.91)	0.235
Blood loss ≥ 100 mL	1.64 (0.48–5.56)	0.430	1.41 (0.42–4.75)	0.583
Cardiac dysrhythmia	1.94 (0.29–12.95)	0.493	0.70 (0.11–4.67)	0.714
Pulmonary complications¶	3.67 (0.63–21.45)	0.149	0.79 (0.16–4.04)	0.779
VCP	15.33 (1.71–137.40)	0.015	13.54 (1.52–120.85)	0.020
Overall complications	7.00 (1.57–31.18)	0.011	2.22 (0.59–8.34)	0.240
Clavien–Dindo grade 3–4 (vs. 0–2)	1.22 (0.16–9.56)	0.848	1.11 (0.14–8.64)	0.924
Fast track program	0.40 (0.10–1.49)	0.171	0.45 (0.12–1.70)	0.240
Length of postoperative stay > 8 days	1.40 (0.42–4.62)	0.581	3.71 (1.06–12.98)	0.040
Perioperative serum parameters				
Preoperative serum PA < 200 mg/L	0.69 (0.21–2.28)	0.545	0.58 (0.18–1.91)	0.367
Preoperative serum A < 43.5g/L	1.00 (0.31–3.28)	1.000	0.58 (0.18–1.91)	0.367
POD1 serum PA < 150 mg/L	1.00 (0.31–3.28)	1.000	0.83 (0.26–2.72)	0.763
POD1 serum A < 33.0 g/L	1.33 (0.39–4.57)	0.647	0.61 (0.18–2.09)	0.428
POD7 serum PA < 110 mg/L††	5.67 (1.55–20.79)	0.009	1.43 (0.44–4.69)	0.555
POD7 serum A < 36.5 g/L††	3.00 (0.87–10.30)	0.081	0.82 (0.25–2.69)	0.741

*The former is the number and rate of the severe weight loss (SWL) group, and the latter is the number and rate of the normal weight change group. †Defined as weight loss > 7.5% of preoperative body weight four weeks after surgery. ‡Defined as weight loss > 13.0% of preoperative body weight one year after surgery. §High fat-free mass (FFM) was defined as >50.0 kg for men and >38.0 kg for women for women. ¶Pulmonary complication was defined as pneumonia, pleural effusion, or acute respiratory distress syndrome (ARDS). ††Data were missing for three patients. A albumin; ASA American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECOG PS, Eastern Cooperative Oncology Group performance status; KPS, Karnofsky Performance Status; OR, odds ratio; PA, pre-albumin; POD, post-operative day; pTNM, pathological tumor node metastasis; SWL, serious weight loss; VCP, vocal cord paralysis.

$P = 0.015$), overall complications (OR 7.00; $P = 0.011$), and serum pre-albumin on the seventh day after surgery < 110 mg/L (OR 5.67; $P = 0.009$) were associated with short-term SWL. The fast-track program showed a trend of decreased risk of short-term SWL (OR 0.40; $P = 0.171$), but this decrease was not statistically significant. The parameters with $P \leq 0.200$ in univariate analysis were included in the multivariate logistic regression model, and the outcomes showed that age ≥ 70 years (OR 7.65; $P = 0.030$), preoperative sarcopenia (OR 7.18; $P = 0.030$), the first surgery in the daily schedule (OR 6.87; $P = 0.032$) and VCP (OR 12.30; $P = 0.046$) were independent risk factors for short-term SWL after esophagectomy (Table 5).

Risk factors for long-term (1 year) severe weight loss after esophagectomy

The average and median of the body weight loss rate one year after surgery were 13.1% ± 6.5% and 12.6% (8.8–17.7%), respectively. Thus, we defined long-term SWL as a body weight loss > 13%. Ultimately, 21 (47.7%) patients belonged to the SWL group and 23 (52.3%) to the NWL group. According to the outcomes of univariate analysis shown in Table 4, cerebral vascular disease ($P = 0.020$), an American Society of Anesthesiologists (ASA) score of 3–4 (OR 4.60; $P = 0.020$), a high PBW (> 66.0 kg for men or > 55.0 kg for women, OR 3.72; $P = 0.040$), high FFM (> 50.0 kg for men or > 38.0 kg for women, OR 7.08; $P = 0.004$), a moderately differentiated tumor (OR 13.00; $P = 0.026$), VCP (OR 13.54; $P = 0.020$), and the length of postoperative stay (LOS) > 8 days (OR 3.71; $P = 0.040$) were associated with SWL one year after surgery. The multivariate logistic regression model demonstrated that an ASA score of 3–4 (OR 6.58; $P = 0.047$), high FFM (OR 21.91; $P = 0.003$), and VCP (OR 25.83; P=0.017) were independent risk factors leading to long-term SWL after esophagectomy (Table 5).

Table 5 Outcomes of multivariate analysis of the risk factors for SWL

Risk factors	OR	95% CI	*P*
Short-term (4 weeks) SWL (n = 20)†			
Age ≥ 70 years	7.65	1.22–48.13	0.030
Preoperative sarcopenia	7.18	1.22–42.38	0.030
The first surgery in the daily schedule	6.87	1.18–40.14	0.032
VCP	12.30	1.04–144.96	0.046
Long-term (1 year) SWL (n = 21)‡			
ASA score 3–4	6.58	1.03–42.22	0.047
High FFM§	21.91	2.93–163.81	0.003
VCP	25.83	1.80–371.28	0.017

†Defined as weight loss > 7.5% of preoperative body weight four weeks after surgery. ‡Defined as weight loss >13.0% of preoperative body weight one year after surgery. §High fat-free mass (FFM) was defined as >50.0 kg for men and >38.0 kg for women. ASA, American Society of Anesthesiologists; CI, confidence interval; OR, odds ratio; SWL, serious weight loss; VCP, vocal cord paralysis.

Quality of life and weight loss

We studied the impact of postoperative intake-related QOL on short-term and long-term weight loss, respectively (Table 6). No significant difference in baseline QOL was observed between the groups in regard to short-term weight loss, except for a higher prevalence of insomnia ($P = 0.001$) and reflux ($P = 0.017$) in the SWL group. Two weeks after the operation, patients in the SWL group reported statistically significantly more problems with insomnia ($P = 0.032$), appetite loss ($P = 0.006$), dysphagia ($P = 0.001$), eating difficulties ($P = 0.040$), taste issues ($P = 0.016$), coughing ($P = 0.040$), and difficulty talking ($P = 0.002$), with a lower score of emotional functioning ($P = 0.021$) than patients in the NWL group. A significant difference was still observed four weeks after surgery.

In the long-term weight loss analysis, emotional functioning ($P = 0.002$) was significantly lower in patients in the SWL group four weeks after surgery, and they reported more serious symptoms of insomnia ($P = 0.010$), appetite loss ($P = 0.017$), dysphagia ($P = 0.045$), eating difficulties ($P = 0.031$), esophageal pain ($P = 0.043$), taste issues ($P = 0.028$), coughing ($P = 0.002$), and difficulty talking ($P = 0.048$) at that time. While the difference in esophageal pain, coughing, and difficulty talking decreased with time, the differences in other symptoms remained significant within one year after surgery.

Discussion

Previous studies have reported different degrees of postoperative weight loss in esophageal cancer patients. A prospective study including 226 patients showed that 63.7% of patients suffered from weight loss > 10% of the PBW six months after surgery, and 20.4% patients showed weight loss of > 20% of the PBW.[6] Recently, two retrospective studies conducted in Asian countries showed weight loss rates of 10.95% ± 7.50% and 12.9% ± 9.08% of the PBW one year after esophagectomy.[5,18] The results of our prospective study, which included Chinese patients who underwent McKeown-MIE, also demonstrated obvious weight loss one year after surgery, at a rate of 13.1% ± 6.5%. Additionally, consecutive follow-up over a year showed that the first two weeks after discharge represented an accelerated weight loss period. According to our experience and the results of previous studies, at least three factors contributed to this particular term:

1 Poor eating function. Both our patient sample and previous studies reported adverse postoperative eating

Table 6 Patients' SWL and related QOL

Questionnaire scales and items	Short-term (4W) SWL and QOL									Long-term (1Y) SWL and QOL									
	Pre			2W			4W			Pre			4W			12W			48W		
	SWL (*n* = 20)	NWL (*n* = 24)	*P*	SWL (*n* = 20)	NWL (*n* = 24)	*P*	SWL (*n* = 20)	NWL (*n* = 24)	*P*	SWL (*n* = 21)	NWL (*n* = 23)	*P*	SWL (*n* = 21)	NWL (*n* = 23)	*P*	SWL (*n* = 21)	NWL (*n* = 23)	*P*	SWL (*n* = 21)	NWL (*n* = 23)	*P*
EORTC QLQC-30 function scales																					
Emotional functioning	87.9 ± 11.3	90.6 ± 10.2	0.427	79.0 ± 9.7	85.4 ± 7.9	0.021	79.1 ± 11.6	87.1 ± 9.2	0.022	88.1 ± 11.4	90.6 ± 10.1	0.481	80.0 ± 87.7	87.7 ± 8.7	0.002	87.7 ± 6.3	94.2 ± 4.6	0.001	92.9 ± 4.8	94.5 ± 3.9	0.022
EORTC QLQC-30 and QLQ – OES18 symptom scales and items																					
Nausea and vomiting	7.5 ± 8.5	7.0 ± 8.4	0.826	14.2 ± 15.5	6.3 ± 9.6	0.076	15.8 ± 15.7	7.6 ± 9.8	0.077	8.0 ± 8.5	6.5 ± 8.3	0.575	13.5 ± 15.5	9.4 ± 11.0	0.463	6.4 ± 8.3	3.6 ± 7.0	0.240	3.2 ± 6.7	1.5 ± 4.8	0.323
Insomnia	26.7 ± 23.2	5.6 ± 12.7	0.001	26.7 ± 23.2	12.5 ± 19.2	0.032	20.0 ± 20.0	8.3 ± 17.7	0.027	25.4 ± 23.3	5.8 ± 12.9	0.002	20.6 ± 19.6	7.2 ± 17.3	0.010	10.9 ± 14.5	2.9 ± 9.6	0.036	7.9 ± 14.5	1.4 ± 6.9	0.043
Appetite loss	16.7 ± 17.1	11.1 ± 16.0	0.268	28.3 ± 27.1	8.3 ± 17.7	0.006	36.7 ± 24.0	15.3 ± 24.0	0.004	17.4 ± 17.0	10.1 ± 15.6	0.144	34.9 ± 26.8	15.9 ± 22.2	0.017	27.0 ± 17.1	10.1 ± 15.7	0.022	14.3 ± 16.9	3.4 ± 6.9	0.033
Constipation	3.3 ± 10.2	4.2 ± 11.2	0.797	3.3 ± 10.2	9.7 ± 15.5	0.121	5.0 ± 12.2	12.5 ± 16.5	0.099	6.3 ± 13.4	1.4 ± 6.9	0.129	7.9 ± 14.5	10.1 ± 15.7	0.626	6.3 ± 13.4	7.2 ± 14.0	0.827	4.8 ± 11.9	2.9 ± 9.6	0.564
Diarrhea	1.7 ± 7.4	2.8 ± 9.4	0.666	5.0 ± 12.2	5.6 ± 12.7	0.882	15.0 ± 20.2	13.9 ± 19.4	0.858	1.6 ± 7.3	2.9 ± 9.6	0.609	11.1 ± 19.2	17.4 ± 19.8	0.195	7.9 ± 18.0	10.1 ± 18.6	0.607	4.8 ± 11.9	2.9 ± 9.6	0.564
Dysphagia	13.9 ± 7.1	12.0 ± 8.0	0.443	31.6 ± 6.5	23.1 ± 8.6	0.001	30.0 ± 12.0	21.3 ± 10.3	0.008	14.4 ± 8.0	11.6 ± 7.1	0.213	28.5 ± 11.9	22.2 ± 11.1	0.045	18.0 ± 6.5	13.5 ± 6.7	0.042	12.2 ± 6.0	8.7 ± 5.2	0.048
Eating difficulties	16.7 ± 13.0	12.5 ± 9.2	0.355	26.3 ± 12.2	18.1 ± 11.9	0.040	27.5 ± 14.6	18.1 ± 14.2	0.039	17.8 ± 13.0	11.2 ± 8.2	0.094	27.0 ± 14.9	18.1 ± 14.1	0.031	16.3 ± 11.0	8.0 ± 9.2	0.035	8.7 ± 12.2	2.4 ± 3.2	0.037
Reflux	19.2 ± 16.5	9.7 ± 14.7	0.017	2.5 ± 6.1	6.3 ± 8.3	0.099	11.7 ± 11.0	13.2 ± 12.0	0.698	18.3 ± 10.4	10.2 ± 19.3	0.002	13.5 ± 11.3	11.6 ± 11.7	0.533	15.1 ± 9.0	14.5 ± 10.4	0.811	11.9 ± 11.9	10.2 ± 9.7	0.695
Esophageal pain	8.3 ± 8.7	6.5 ± 8.6	0.436	11.7 ± 8.4	11.1 ± 8.0	0.819	11.1 ± 8.1	13.9 ± 8.2	0.259	7.9 ± 7.9	6.8 ± 9.3	0.485	10.0 ± 7.8	15.0 ± 7.9	0.043	7.4 ± 6.4	4.3 ± 6.5	0.093	3.7 ± 5.4	1.4 ± 3.8	0.113
Difficulty swallowing saliva	10.0 ± 15.7	9.7 ± 15.5	0.952	18.3 ± 20.2	9.7 ± 15.5	0.138	13.3 ± 16.7	5.6 ± 12.7	0.087	9.5 ± 15.4	10.1 ± 15.7	0.894	12.7 ± 16.6	5.8 ± 12.9	0.128	11.1 ± 16.1	4.3 ± 11.5	0.113	6.3 ± 13.4	2.9 ± 9.6	0.323
Choke when swallowing	16.7 ± 20.2	16.7 ± 17.0	0.871	23.3 ± 15.7	13.9 ± 16.8	0.063	16.7 ± 17.1	11.1 ± 16.0	0.268	15.9 ± 17.0	17.4 ± 19.8	0.882	17.4 ± 17.0	10.1 ± 15.7	0.144	12.7 ± 16.6	5.9 ± 9.6	0.222	7.9 ± 14.5	2.4 ± 6.9	0.163
Dry mouth	18.3 ± 20.2	15.3 ± 16.9	0.676	26.3 ± 13.9	20.3 ± 19.4	0.209	13.3 ± 16.7	16.7 ± 19.7	0.624	22.2 ± 19.2	11.6 ± 16.2	0.062	14.3 ± 16.9	15.9 ± 19.8	0.871	14.3 ± 16.9	7.2 ± 14.0	0.138	7.9 ± 14.5	4.3 ± 11.5	0.361
Taste issues	11.7 ± 16.3	8.7 ± 15.0	0.530	43.3 ± 24.4	26.4 ± 19.6	0.016	42.1 ± 26.9	20.2 ± 24.1	0.011	12.7 ± 16.6	7.6 ± 14.3	0.278	40.0 ± 27.8	21.2 ± 24.2	0.028	19.0 ± 19.9	10.3 ± 11.5	0.045	9.5 ± 15.4	3.4 ± 6.9	0.040
Coughing	6.7 ± 13.7	2.8 ± 9.4	0.267	36.7 ± 21.4	23.6 ± 18.3	0.040	25.0 ± 21.3	11.1 ± 18.8	0.021	6.3 ± 13.4	2.9 ± 9.6	0.323	27.0 ± 20.1	8.7 ± 18.0	0.002	14.3 ± 16.9	3.0 ± 9.8	0.012	7.9 ± 14.5	2.4 ± 6.9	0.163
Difficulty talking	3.3 ± 10.2	2.8 ± 9.4	0.850	31.7 ± 27.5	8.3 ± 14.7	0.002	21.7 ± 24.8	6.9 ± 13.8	0.028	1.6 ± 7.3	4.3 ± 11.5	0.345	20.6 ± 24.7	7.2 ± 14.0	0.048	11.1 ± 16.1	2.9 ± 9.6	0.045	6.3 ± 13.4	1.4 ± 6.9	0.129

The scores are presented as mean ± standard deviation. EORTC, European Organization for Research and Treatment of Cancer; NWL, normal weight loss; QOL, quality of life; SWL, severe weight loss.

symptoms, including dysphagia, eating difficulties, trouble swallowing saliva, and choking when swallowing within a short time after esophagectomy.[15,19] These symptoms worsened in the short term after discharge because of the lack of medical guidance but relieved gradually with time.

2 Stress response. Surgical damage, incision scar, new lifestyle after discharge, and residual symptoms (coughing, dysphagia, cracked voice) can cause significant stress responses after discharge, which lead to greater catabolism and energy consumption, severe sleep disorders, and decreased digestive function.[20–22]

3 Gut hormone secretion disorder. Previous studies have shown that patients with esophageal cancer experience a severe decrease in ghrelin secretion and a significant increase in postprandial plasma glucagon-like peptide 1 (GLP-1) and peptide YY (PYY), contributing to severe appetite loss and decreased food intake after esophagectomy.[23–26]

Short-term SWL after esophagectomy has not been extensively studied worldwide. The results of our study show significant differences in risk factors for postoperative short-term and long-term SWL in patients with esophageal cancer, while VCP was the only common independent risk factor. Patients suffering from VCP are reported to experience symptoms of aspiration, which result in eating difficulties and a serious postoperative stress response.[27–29] The impact of this adverse factor may continue for a number of months to several years.[30] Damage to macromolecules in human cells accumulates with age, resulting in the gradual decline of cell function.[31] Older patients are more likely to experience SWL in the short term after surgery because of decreased anabolism and physical dysfunction.[32] Sarcopenia, related to advanced age and malignant tumors, results in weakness and decreased resistance and tolerance.[7] Previous studies have shown that preoperative sarcopenia is a risk factor for mortality, postoperative complications, and poor survival.[33–35] Our results show that this factor also leads to postoperative short-term SWL. Additionally, the first surgery in the daily schedule was associated with short-term SWL, but no significant difference in patient characteristics and perioperative data was observed between the first and following surgery groups (data not shown). Patients in our center who underwent the first surgery in the daily schedule usually entered the preoperative area an hour earlier, and thus may have experienced more serious preoperative anxiety than patients that underwent following surgeries with a shorter wait in the preoperative area. The rate of delay to the start of the scheduled first operation is higher than for the following surgeries, which may influence short-term weight loss. Further studies are warranted to confirm the effect of operation order on patients' postoperative body weight recovery.

The FFM is defined as the main factor determining resting energy expenditure (REE), and allows a person to maintain biological function during resting.[36–38] Patients with a high FFM experience a higher energy requirement during the postoperative chronic recovery term, during which the REE is the main energy expenditure. However, patients are reported to experience hypermetabolism caused by multiple factors in the acute stage after esophagectomy.[39,40] Our results also showed no association between FFM and short-term SWL. Patients with an ASA score of 3–4 always suffer from severe systemic diseases and dysfunction before surgery, which appear to affect not only perioperative complications and mortality but also postoperative weight recovery.[41–43] Previous studies have also investigated the risk factors for SWL after esophagectomy. Park *et al.* reported that preoperative weight and postoperative VCP were independent risk factors for weight loss > 10% of PWL one year after esophagectomy.[18] Harada *et al.* reported that the absence of pyloroplasty was the sole risk factor for > 10% weight loss of PWL one year after esophagectomy.[5] A retrospective study with six months follow-up after esophagectomy showed that preoperative BMI and a shorter LOS resulted in > 10% weight loss.[44] In this study, however, except for VCP, we found no definitive association between the PBW, BMI, and LOS with long-term SWL.

Patients' body weight is always associated with food intake and energy expenditure. Previous studies have reported the detrimental effect of esophagectomy on patients' short-term QOL, particularly in regard to eating.[15,45] But few studies have focused on the impact of eating symptoms on body weight loss. Martin *et al.* reported that eating difficulties, pain, fatigue, nausea and vomiting, and appetite loss were clinically relevant and statistically significantly worse among patients with weight loss of ≥ 15% five years after esophageal cancer surgery.[46] Our results indicate that postoperative esophageal symptoms, including appetite loss, dysphagia, eating difficulties, and taste issues are related to both short-term and long-term SWL, mainly because of their detrimental effect on food intake. Patients suffering from insomnia are not likely to get proper rest, which contributes to SWL.[47] Additionally, patients that experienced SWL reported worse emotional functioning, indicating tension, anxiety and depression, which were related to stress response and energy expenditure.[48] There is surely complex interaction among eating symptoms, insomnia, emotional functioning, and weight loss, revealing the need for postoperative life guidance and nutrition intervention for esophageal cancer patients.

In this study, we prospectively observed changes in the body weight of 44 patients with esophageal cancer one year after surgery and propose the existence of an accelerated weight loss period in the first two weeks after discharge.

We also investigated the risk factors for SWL at four weeks and one year after surgery. However, there were limitations to this study. Only a small sample of Asian patients during the short term was analyzed, and the pathological type of the tumor was mainly SCC. Patients who underwent neoadjuvant therapy followed by esophagectomy were excluded, and all of the patients in this study underwent McKeown MIE. Thus, the effects of multi-treatment and surgical methods on weight recovery require further exploration.

Acknowledgments

The study was funded by the Top Talent Fund for Medical Science and Technology (Grant no. 3101030102) and the Key Science and Technological Breakthrough Project of Henan Province (Grant no: 152102310160). We would like to thank M.K. Ferguson (Department of Surgery, The University of Chicago Medicine, Chicago, Illinois, USA) for providing advice and sharing data.

Disclosure

No authors report any conflict of interest.

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