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Analysis of Factors Associated with Weight Loss After Esophagectomy for Esophageal Cancer

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Abstract. *Aim: To investigate the factors associated with weight loss (WL) after esophagectomy for esophageal cancer. Patients and Methods: We retrospectively reviewed 136 patients who underwent esophagectomy for esophageal cancer. Preoperative characteristics, surgical methods, postoperative outcomes and weight changes at 6 months after surgery were analyzed. Results: Seventy-eight patients had more than 10% WL compared to their weight at surgery. On univariate analysis, higher body mass index [(BMI): ≥20.8; p=0.012] and shorter length of hospitalization [(LOH); p=0.041] demonstrated an association with more than 10% WL. On multivariate analysis, higher BMI [odds ratio (OR)=2.821; 95% confidence interval (CI)=1.238-6.426; p=0.014] and shorter LOH (OR=2.953; 95% CI=1.009-8.646; p=0.048) were independently associated with more than 10% WL. Conclusion: Higher BMI and shorter LOH were unfavorable risk factors for WL after esophagectomy for esophageal cancer.*

Esophagectomy is the standard treatment for esophageal cancer (1); however, it has a high risk of postoperative complications and mortality (2). Thoracic esophagectomy with radical lymphadenectomy, using the right thoracic and abdominal approach, followed by gastric tube reconstruction through the retro-sternum or posterior mediastinum route is commonly performed for thoracic esophageal cancer (3). This is an invasive treatment due to the wide surgical field.

Recently, less invasive esophagectomy by means of thoracoscopy or laparoscopy procedures have been used worldwide (4-6). The short-term benefits of these less invasive techniques include lower operative blood loss volume and shorter postoperative hospitalization; however, long-term benefits, such as survival and quality of life (QOL), are still unclear (7). Concerning patient QOL after esophagectomy, the extent of body weight change is important. Several adverse changes in the daily diet occur after esophagectomy because of decreased stomach capacity or swallowing dysfunction due to anastomotic stenosis. Even using postoperative enteral nutrition support, postoperative weight loss (WL) is still problematic. In addition, postoperative WL of more than 10% might affect survival after esophagectomy for esophageal cancer (8). Therefore, preventing WL after esophagectomy is important for patients' QOL and survival. The aim of this study was to investigate the significant factors associated with WL after esophagectomy for esophageal cancer.

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Key Words: Weight loss, esophagectomy, esophageal cancer.

Patients and Methods

We retrospectively reviewed 136 patients who underwent esophagectomy using the thoraco-abdominal approach for esophageal cancer from April 1999 to April 2014. We reviewed their weight changes until 1 year after surgery. We assessed the following patients' characteristics: age; gender; stage; neoadjuvant chemotherapy; nutrition status, including body mass index (BMI) and serum albumin level; surgical methods, including surgical approach (thoracoscopic esophagectomy or not); reconstruction route [posterior mediastinum or other); conduit (gastric tube or other); anastomosis method (hand-sewn or stapler); postoperative outcomes (anastomotic leakage and length of hospitalization (LOH)]; and adjuvant treatment (chemotherapy or chemoradiotherapy). We also reviewed their weight changes at 1, 3, 6 and 12 months after surgery and divided the patients into two groups according to their WL at 6 months after the surgery (more than 10% decreased or not).

Surgical methods. From April 2004 to June 2009, we performed right thoracotomy using a laparoscopic approach (9). In July 2009, we introduced thoracoscopic esophagectomy in the prone position (7) and made several changes to the anastomosis technique. Until June 2001, we performed cervical esophago-gastric tube anastomosis using the hand-sewn technique. In June 2001, we began performing cervical anastomosis using a circular stapler. In October 2004, we began performing intra-thoracic anastomosis using a circular stapler. In October 2005, we returned to using the cervical hand-sewn method until September 2009. Since then, we have routinely performed cervical anastomosis using a circular stapler. In 2011, we introduced the indocyanine green fluorescence method during use of the gastric tube to visualize the blood supply (10). A feeding jejunostomy catheter was inserted in all patients.

Statistical analysis. For statistical analyses, patients were stratified into WL groups of less than 10% and 10% or more according to their WL at 6 months after the surgery. We assessed the difference between the mean values for the two groups by using the Mann-Whitney *U*-test for continuous variables and the Chi-square test for categorical variables. The Kaplan-Meier method and log-rank test were used to compare the cumulative survival rates. Logistic regression analysis was used to identify factors associated with more than 10% WL at 6 months after surgery (6M10%WL). Statistical analysis was performed using JMP 6 (SAS Institute Inc., Cary, NC, USA).

Results

There were 107 male and 29 female patients. The median age of patients was 65 years. Cancer stages according to the TNM classification of malignant tumors, 7th edition, were as follows: stage I, 45 patients (33.1%); stage II, 24 patients (17.6%); stage III, 58 patients (42.6%); and stage IV, 9 patients (6.6%). Neoadjuvant chemotherapy, which was introduced in 2009, was performed for 56 patients (41.2%). Twelve patients (8.8%) had more than 10% WL before surgery; their median BMI was 20.8. Eight patients (5.9%) had low serum albumin levels (<3.5 mg/dl). Thoracoscopic esophagectomy was performed for 64 patients (47.1%). Gastric tube reconstruction (n=129; 94.9%) through the posterior mediastinum route (n=116; 85.3%) was mainly performed. Only seven patients underwent colon (n=6) or jejunum (n=1) reconstruction. Hand-sewn anastomosis was performed for 56 patients (41.2%). A stapler was used for 80 patients (58.8%). Anastomotic leakage occurred in 19 patients (14.0%). The median LOH was 28 days and adjuvant therapy was performed for 74 patients (54.4%).

The weights decreased until 6 months after surgery and remained stable until 12 months after surgery. The mean weight of patients at 1, 3, 6 and 12 months after surgery compared to weight at surgery was 95.1±7.9%, 90.5±8.7%, 89.2±10.4% and 88.2±14.3%, respectively. Seventy-eight patients (57.4%) had 6M10%WL. Table I summarizes patients with and without 6M10%WL. On univariate analysis, higher preoperative BMI (≥20.8; p=0.012) and shorter LOH (p=0.041) demonstrated an association with 6M10%WL. On multivariate analysis, higher preoperative BMI (odds ratio (OR)=2.821; 95% confidence interval (CI)=1.238-6.426; p=0.014) and shorter LOH (OR=2.953; 95% CI=1.009-8.646, p=0.048) were independently associated with 6M10%WL (Table II). Survival of patients whose WL at 6 months after surgery was 10% or more tended to be poorer than that of patients with WL less than 10% at 6 months after surgery, although there was no significant difference between the two groups (p=0.226).

Table I. *Univariate analysis of patients with weight loss at 6 months after esophagectomy.*

Variables	Weight loss <10% N=58	Weight loss ≥10% N=78	*p*-Value
Age, <65/≥ 65	38/20	34/44	0.112
Gender, M/F	40/18	61/17	0.766
Stage, I/II/III/IV	18/7/23/3	24/16/34/4	0.977
Preoperative treatment (%)	16 (27.6)	38 (48.7)	0.182
Preoperative weight loss ≥10% (%)	7 (12.1)	5 (6.4)	0.347
Body mass index ≥20.8 (%)	22 (37.9)	48 (61.5)	<0.012
Albumin <3.5 mg/dl (%)	4 (6.9)	4 (5.1)	0.900
Thoracoscopic esophagectomy (%)	17 (29.3)	42 (53.8)	0.105
Gastric tube reconstruction (%)	49 (84.5)	74 (94.9)	0.993
Posterior mediastinum route (%)	43 (74.1)	68 (87.2)	0.738
Hand-sewn anastomosis (%)	23 (39.7)	30 (38.5)	0.395
Anastomotic leakage (%)	8 (13.8)	9 (11.5)	0.102
Hospitalization ≤28 days (%)	26 (44.8)	39 (50.0)	0.041
Adjuvant therapy (%)	24 (41.4)	47 (60.3)	0.065

Table II. *Multivariate analysis of patients with weight loss >10% at 6 months after esophagectomy.*

Variables	OR	95% CI	*p*-Value
BMI ≥20.8	2.821	1.238-6.426	0.014
Hospitalization ≤28 days	2.953	1.009-8.646	0.048

OR, Odds ratio; CI, confidence interval; BMI, body mass index.

Discussion

We found that the weights of surgical patients decreased until 6 months after esophagectomy and that higher preoperative BMI (≥20.8) and shorter LOH (≤28 days) were significant risk factors associated with 6M10%WL after esophagectomy for esophageal cancer. Martin *et al*. (11) also reported that preoperative BMI of 25 or higher was a risk factor (OR=3.2; 95% CI=1.4-7.3) for postoperative WL (≥15%), even at 5 years after surgery. Zhang *et al*. (12) reported that higher BMI was a risk factor for anastomotic leakage; however, it was associated with favorable survival compared to that of patients with normal weights (hazard ratio (HR)=0.80; 95% CI=0.70-0.92; p=0.001). On the contrary, van der Schaaf reported that preoperative WL (>10%) was a risk factor for poor survival (HR=1.34; 95% CI=1.02-1.74; p=0.001) (13). These results might reflect the correlation between BMI and cancer stage. Preoperative weights of patients with advanced esophageal cancer tended to be lower than those of patients with non-advanced cancer due to esophageal stenosis (14). In the present study, preoperative BMIs of clinical T3 or T4 patients were significantly lower than those of T1 patients (20.7±3.2 *vs*. 22.2±3.5; p=0.028).

Some researchers have reported an association between postoperative WL and poor survival. D'Journo *et al*. (8). reported that postoperative WL (12 months after surgery) of more than 10% was associated with poor disease-free survival (HR=2.1; 95% CI=1.2-3.4; p=0.004), as well as N stage and non-curative surgery. In gastric cancer, postoperative WL was reported as an independent risk factor for continuation of adjuvant chemotherapy (15). However, in the present study, patients' weights at 6 months after surgery between the T1 and T3 or T4 patients were not significantly different (89.2±7.4% *vs*. 89.1±9.9%; p=0.961) and 6M10%WL was not associated with a poor prognosis.

We routinely used needle catheter feeding jejunostomy and enteral nutrition after esophagectomy. We recommended self-enteral nutrition until oral diet intake could be sufficient, even for patients who were discharged from the hospital. This was useful for maintaining body weight during postoperative management and home support (16). In the present study, shorter LOH was associated with postoperative WL. The main reason for prolonging LOH was postoperative complications, especially anastomotic leakage. When leakage occurred, we performed drainage and increased enteral nutrition. Patients with longer LOH who were administered enteral nutrition for a longer period had less WL.

There have been some reports about the correlation between postoperative WL and gut hormones, including ghrelin (17, 18). Recently, a Japanese traditional medicine called rikkunshito (TJ-43) has been investigated as a ghrelin enhancer and as an enhancer of synergistic or direct stomach action (19). Postoperative TJ-43 might help patients maintain body weight after esophagectomy.

We recognize that this study has some limitations because of its retrospective design, as well as being a single institution study. Further investigation is necessary to clarify the impact of postoperative WL and effective support, including enteral nutrition or TJ-43, in patients who undergo esophagectomy. The present study demonstrated that patients' WL continued until 6 months after esophagectomy and higher preoperative BMI and shorter LOH were predictors of postoperative WL. These results might contribute to increasing the use of adequate postoperative nutrition support for patients with esophageal cancer, even if they had no complications and experienced improvement early after esophagectomy.

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Conflicts of Interest

None.

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