Clinical Significance of Weight Changes in Malnutrition After Oesophagectomy for Cancer

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Research

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Abstract

Purpose

This aim of study was to evaluate the potential effect of differences in body mass index (BMI) on nutritional status of patients after esophagectomy.

METHODS

We retrospectively analyzed the association of BMI changes associated with nutritional dysfunction among esophageal cancer patients who received R0 esophagectomy from 2018 to 2019. The odd ratio (ORs) of factors related to more than 15% weight loss compared with the body weight at the discovery of the esophageal cancer and 95% confidence intervals (CIs) were estimated via binary logistic regression models after adjusting possible confounders.

RESULTS

This study included 145 patients with median age at surgery 59 (interquartile range [IQR] 28–81 years), 44 female (43.6%), and mean BMI 25.1 ± 5.3 Kg/m2 at the onset of the disease. At 1-year follow-up, 33 patients (22.8%) experienced ≥ 15% weight loss: 20 among the 52 patients with BMI ≥ 25 kg/m2 and 13 among the 93 patients with BMI < 25 kg/m2 at the onset of the disease (P = 0.023). After adjustment for potential confounders, initial overweighting as well as advanced tumour p-stage were independent risk factors for higher risk of 1-year ≥ 15% weight loss (OR 2.07, 95%CI (1.39, 3.08); P=0.041; OR 2.58, 95% CI (1.64, 4.06); P=0.032).

CONCLUSION

Association exists between overweighting at the onset of the disease and postoperative ≥ 15% weight loss risk in patients with oesophagectomy, highlighting the modulation and control of body weight to reduce the risk of malnutrition following oesophagectomy.

Introduction

Esophageal cancer is a more common type of digestive system tumor, with an increasing trend of the incidence year by year [1]. China is a high incidence of esophageal cancer and one of the highest mortality rates of esophageal cancer in the world, carrying more than half of the total number of deaths from esophageal cancer in the world every year [2]. At present, esophagectomy is the first choice in the therapies of esophageal cancer. However, due to the change in digestive function and imbalance in nutritional status, as well as stress and injury caused by perioperative procedures, the patients' life qualities are severely affected [3].

Malnutrition is a common problem in patients with cancer, and its incidence rate is up to 40% ~ 80%, and esophageal cancer is the disease with the one of the highest incidence of malnutrition among these

malignant tumors [4]. Patients with esophageal cancer usually have eating disorders and different degrees of malnutrition before surgery. After radical resection of esophageal carcinoma, the nutritional status of the patients was further deteriorated mainly due to surgical trauma and long-term fasting in addition to high consumption after surgery [5]. At the same time, patients with esophageal cancer are greatly impacted psychologically and mentally, which also directly affect the quality of life of patients [6].

Recent clinical studies have shown that approximately 50% patients lose more than 20 % body weight within 6 months of esophagectomy [7]. Previous studies suggested that recurrence, overweight and postoperative complications were likely to be associated with postoperative malnutrition [8]. However, knowledge is little regarding the reasons for such weight loss.

The primary objective was to estimate the association of differences in body mass index (BMI) at the very start of esophageal cancer and the risk of postoperative ≥ 15% weight loss in patients with oesophagectomy. The secondary objective was to identify the potential independent risk factors of developing malnutrition following oesophageal cancer surgery.

Patients And Methods

Study design and population

Oesophageal center of the First Affiliated Hospital of Nanjing Medical University is a regional provincial professional esophageal cancer treatment center, in which esophageal patients underwent surgical and/or multidisciplinary therapy. Between January 1, 2018 and December 31, 2018, consecutive patients from the esophageal center with esophageal cancer were retrospectively included if they underwent R0 transthoracic oesophagectomy. The Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University approved the study protocol. This study followed the Declaration of Helsinki. Due to the nature of this retrospective study, the Institutional Review Board waived the need for patient consent.

We identified retrospectively 1-year disease-free survivors, and excluded patients who had an early recurrence of disease, postoperative death at the first 12 months after oesophageal cancer surgery [9]. We also excluded the patient with incomplete resection (R1–R2). Additional exclusion criteria were incomplete surgical records and missing follow-up outcome data for identification of postoperative nutrition dysfunction.

At last, 145 patients were included in this study with 12-month disease-free survivors. The patient was regard as free of disease when postoperative comprehensive examination results were favorable at least including a full-body scan and esophageal endoscopy.

Data Collection

According to the case information system data of the First Affiliated Hospital of Nanjing Medical University, patient demographic data (age, gender, height, weight), and tumor tumour characteristics (pathological type, clinical stage, tumor location), and surgical procedures (surgical approach) were all

collected. Laboratory, radiology, and anesthesiologists and follow-up staffs also assisted in supplementing and perfecting the data. Follow-up data was collected through patient outpatient and inpatient medical records or telephone Internet. The primary endpoints were death, recurrence, metastasis, and weight changes. Clinical and pathological staging was estimated following the system of the International Union Against Cancer [10].

Procedure

According to the protocol of our institute, the standard oesophagectomy included en bloc excision with 2- or 3-field lymph node removals at their discretion of surgeons, gastric tube reconstruction and oesophagogastric anastomosis using the stomach in all patients as described previously [11,12]. Specific surgical procedures were performed according to our previously reported articles [13].

Body mass index

In the present study, BMI was calculated four times during the study period :(1) at the onset of any pre-treatment symptoms prior to treatment (pre-treatment BMI); (2) Before and during surgery (preoperative BMI); (3) Six months after surgery (6-month BMI) and (4) 12 months after surgery (1 year-BMI) [9].

Weight loss assessment

Denutrition was defined as a weight loss ≥15% measured as (weight at the onset of symptoms before any treatment in kilograms - weight at 1 year after oesophageal cancer surgery in kilograms)/ weight at the start of symptoms without any intervention in kilograms. Patients were divided into groups who experienced a weight loss < 15% of the pretreatment body weight and those with a weight loss ≥ 15% of the pre-treatment body weight [9].

Statistical analysis

Continuous data were presented as mean (SD) or median (IQRs) and compared using a t-test or Kruskal-Wallis testing according to distributed characteristics, and categorical data were presented as percentages (%) and compared using $\chi 2$ testing. The odd ratio (ORs) of factors of 1-year body weight loss ≥ 15% and 95% confidence intervals (CIs) were analyzed by binary logistic regression models. Baseline adjustments for age at surgery, sex, BMI, histology, tumour stage, tumour location, neoadjuvant treatment, jejunostomy, complications, and surgery mode. All covariates showing relative strong associations (p value <0.1) with 1-year body weight loss ≥ 15% in univariate analysis were modelled together to investigate independent risk factors of1-year body weight loss ≥ 15% using multivariate logistic regression. Statistical analyses were performed by R software (version 3.2.0). P <0.05 were considered statistically significant.

Results

Patient characteristics

This study included 145 patients received a R0 transthoracic oesophagectomy, with median age at surgery 59 (IQR 28–81 years), 44 female (43.6%), and mean BMI 25.1 ± 5.3 Kg/m2 at the onset of the disease. Table 1 summarizes the main characteristics and clinical details of the 145 patients.

Body mass index

At the initial stage of disease detection, majority of patients (n = 58.6%) had a pre-treatment BMI ranging between 18.5 and 24.9 Kg/m2. The mean pre-treatment BMI was 25.1 ± 5.3 Kg/m2 and ranged from 16.2 Kg/m2 to 34.5 Kg/m2. Among the remaining 60 patients, 38 patients have a pre-treatment BMI of ≥ 25 Kg/m2, 14 patients have a pre-treatment BMI of ≥ 30 Kg/m2 and 8 patients have a pre-treatment BMI of < 18.5 kg/m². Assessment of BMI trajectory in the study period is presented in Table 2.

Weight loss outcome

Compared with BMI felt to 24.0 ± 4.8 kg/m2 at the time of surgery, 21.7 ± 4.5 kg/m2 at postoperative 6 months, and 22.3 ± 4.8 kg/m2 at 1 year after oesophagectomy. Among the 145 patients, 36 (24.8%) have experienced an unintentional preoperative weight loss ≥ 10% before R0 transthoracic oesophagectomy. At 6 months after oesophagectomy, 42 (31.7%) patients experienced a ≥ 15% weight loss compared with pre-treatment body weight. At 1 year after oesophagectomy, 33 patients (22.8%) experienced a ≥ 15% weight loss: 20 among the 52 patients with BMI ≥ 25 kg/m2 and 13 among the 93 patients with BMI < 25 kg/m2 at the onset of the disease (P = 0.023). During the follow-up period of this present study, the trajectory of weight loss in male patients was similar to those in female patients (Figure. 1); the trajectory of weight loss in patients without having a neoadjuvant therapy was also similar to those in female patients having received a neoadjuvant therapy (Figure. 2).

Risk factor analysis

All potential related variables (P<0.10) in the univariable analysis were entered into the logistic regression model. The multivariate analysis indicated that age, sex, tumour location, histology of tumor, neoadjuvant treatment, feeding Jejunostomy, weight loss before surgery, and occurrence of postoperative complications had little association with a 1-year weight loss ≥15% of the pre-treatment body weight. After adjustment for baseline, clinical and procedural variables, patients with initial overweighting as well as advanced tumour p-stage were associated with higher risk of 1-year ≥ 15% weight loss (OR 2.07, 95%CI [1.39, 3.08]; P=0.041; OR 2.58, 95% CI [1.64, 4.06]; P=0.032) (table 3).

Discussion

Our findings show that significant association exists between initial overweighting at the onset of the disease and 1-year follow-up ≥ 15% weight loss risk in patients with oesophagectomy after adjustment for potential variables. After adjustment for baseline, clinical and procedural variables, patients with initial overweighting as well as advanced tumour p-stage were independent risk factors for higher risk of 1-year ≥ 15% weight loss. There were some indications that patients who received oesophageal resection

for cancer were associated with a trend towards increased risk of postoperative denutrition. It highlights the modulation and control of body weight to reduce the risk of malnutrition following oesophagectomy.

Interpretation and implications

Current evidence suggests that cancer patients undergoing major surgery have a higher risk of malnutrition [15]. For patients with digit-gastrointestinal cancer, the impact of larger operations on postoperative nutrition is often more severe. It is suggested that in gastrointestinal surgery, preoperative body weight has an important influence on postoperative nutritional status, and is also an important predictor of long-term postoperative nutritional deficiency [16]. In this study, these patients with initial overweighting was associated with higher risk of 1-year ≥ 15% weight loss (OR 2.07, 95%CI [1.39, 3.08]; P=0.041), which is consistent with their previous results [9], which provided evidence verifying impaired initial overweighting closely correlating with poor weight loss after oesophageal resection for cancer. Thus, it highlights the therapeutic modalities of body weight not only after and during oesophagectomy but also at the onset of the disease and before any treatment in the management of nutrition in oesophageal resection for cancer [17].

Weight loss and postoperative denutrition is not a single but multifactorial factor in etiology, including surgical trauma, anesthesia, physical stress, psychological stress during the operation [18]. Studies have speculated that weight loss in patients with esophageal cancer after surgery is usually associated with the redistribution and activation of the patient's own immune system [19]. A severe but self-limited systemic inflammatory response usually follows major gastrointestinal surgery. Patients with severe postoperative complications are often hit twice: on the one hand by the surgery itself, and on the other by secondary complications and other adverse events. Therefore, the correlation between patients' immune function status and postoperative nutrition should be further investigated in future basic and clinical studies [20]. Importantly, different from other common operations, esophageal cancer surgery requires patients to fast for a long time after the operation, which will further aggravate the nutritional disorders of the patients. Consequently, accurate assessment of perioperative risk by considering the potential risk of surgical procedures and patient clinical characteristics will lead to a timely and accurate use of nutrition management and weight control for a better identification and management of patients as risk for or in a state of postoperative weight loss and postoperative denutrition [21].

There are always more solutions than problems. The best solution for postoperative severe malnutrition should be reasonable and continuous enteral nutritional support after one month of the operation of esophageal cancer, so as to control and reduce the risk of postoperative nutritional disorders and stunting. Feeding jejunostomy has been proven to be an effective and economical way to provide preoperative and long-term support to patients with esophageal cancer [22]. However, there is still no consensus on the application time and duration of enteral nutrition [23]. Our findings suggested significant association of initial overweighting at the onset of the disease with 1-year follow-up ≥ 15% weight loss risk following oesophagectomy. As far as we are concerned, future studies should focus on

whether prolonged enteral nutritional support especially for overweight patients as well as its possible mechanism of action [24].

There were some limitations in this present study when interpreting our results. First of all, due to the retrospective design, attention should be paid to an inherent bias in our study regarding the evidence grade. Even though general baseline characteristics before surgery were equally distributed among the groups, we were unable to completely exclude all confounders which is likely to interfere with our findings. Despite multivariable adjustments for measured factors for this analysis, the residual bias from unmeasured factors and effect-modifying potentials cannot be completely excluded. Besides, the findings could be confounded and should be interpreted with caution as they were based on a single center.

Conclusion

Our findings showed initial overweighting at the onset of the disease was associated with risk of 1-year follow-up ≥ 15% weight loss risk in patients with oesophagectomy, highlighting the modulation and control of body weight to reduce the risk of malnutrition following oesophagectomy. Also, patients with initial overweighting as well as advanced tumour p-stage were independent risk factors for higher risk of 1-year ≥ 15% weight loss. However, the unmeasured factors with confounding and effect-modifying potentials affecting myocardial dysfunction cannot be excluded.

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate: The study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University.

Consent for publication: All authors have approved the submitted manuscript.

Competing interests: The authors declare that they have no competing interests.

Availability of data and materials: Not applicable.

Competing interests: none

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Authors' contributions: JF design research, writing thesis. All authors collected and analyze the data. JL reviewed and edited the manuscript.

All authors read and approved the manuscript.

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Tables

Table 1: Characteristics and clinical details of 1-year disease-free survivors

Characteristics and clinical details	N=145
Age, year	
<60	72
60–69	47
≥70	26
Sex ratio (male/female)	101/44
Histology	
Adenocarcinoma	89
Squamous cell carcinoma	56
Tumour stage	
0	20
I	40
II	53
III	32
Tumour location	
Upper oesophagus	5
Middle oesophagus	32
Lower oesophagus	108
Neoadjuvant treatment	
No	87
Yes	58
Jejunostomy	
No	65
Yes	80
Complications (Clavien classification)	
None (stage 0)	61
Minor (stages: 1, 2)	55
Major (stages: 3, 4)	29
Surgery	

Ivor Lewis	111
Left thoraco-abdominal approach	10
Mac Keown	24

Table 2: Weight characteristics and BMI variations of patients within one year

Variables	N=145
Pre-treatment BMI	
Underweight (BMI < 18.5)	8 (5.5%)
Normal (BMI 18.5–24.9)	85 (58.6%)
Overweight (BMI 25–30)	38 (26.2%)
Obese (BMI ≥ 30)	14 (9.7%)
Preoperative weight loss(%)	
<10	109 (75.2%)
≥10	36 (24.8%)
Mean of body mass index (kg/m²)	
Pretreatment	25.1 ± 5.3
Preoperative	24.0 ± 4.8
Six months after operation	21.7 ± 4.5
1 year after operation	22.3 ± 4.8
6-months postoperative WL	
<15%	103 (68.3%)
≥15%	42 (31.7%)
1-year postoperative WL	
<15%	112 (77.2%)
≥15%	33 (22.8%)

Table 3: Multivariate analysis of factors associated with a 1-year weight loss ≥15% after oesophageal cancer resection

	OR (95%CI)	P value
Age	1.46 (0.86, 2.49)	0.19
Sex (male)	0.87 (0.64, 1.18)	0.68
Histology	1.21 (0.79, 1.85)	0.55
Jejunostomy	1.35 (0.95, 1.91)	0.32
Postoperative complications	1.86 (0.83, 4.19)	0.17
p-T stage	2.07 (1.39, 3.08)	0.041
Pre-treatment BMI > 25	2.58 (1.64, 4.06)	0.032

Multivariable model including adjustments for age, sex, tumour stage, histological type, complications, neoadjuvant therapy, preoperative weight loss, pre-treatment BMI.

Figures

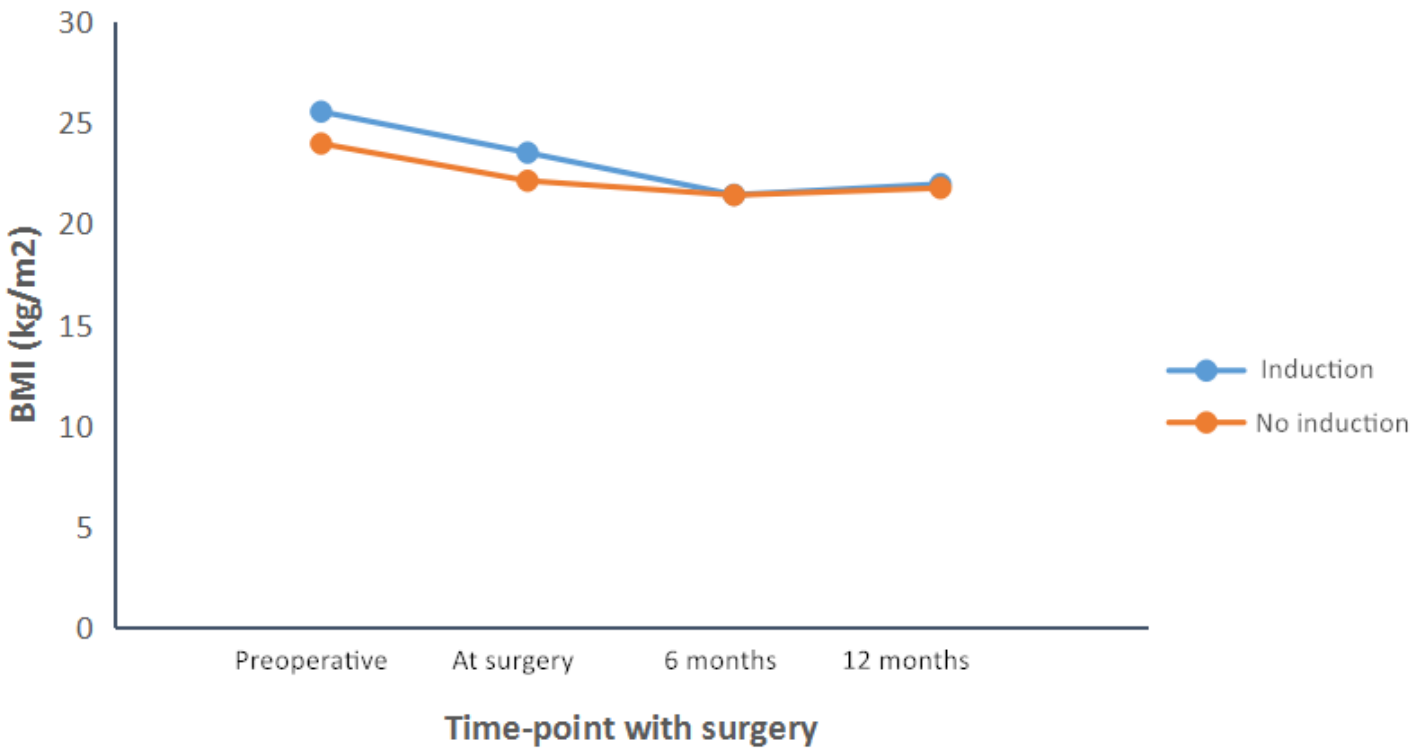

Figure 1

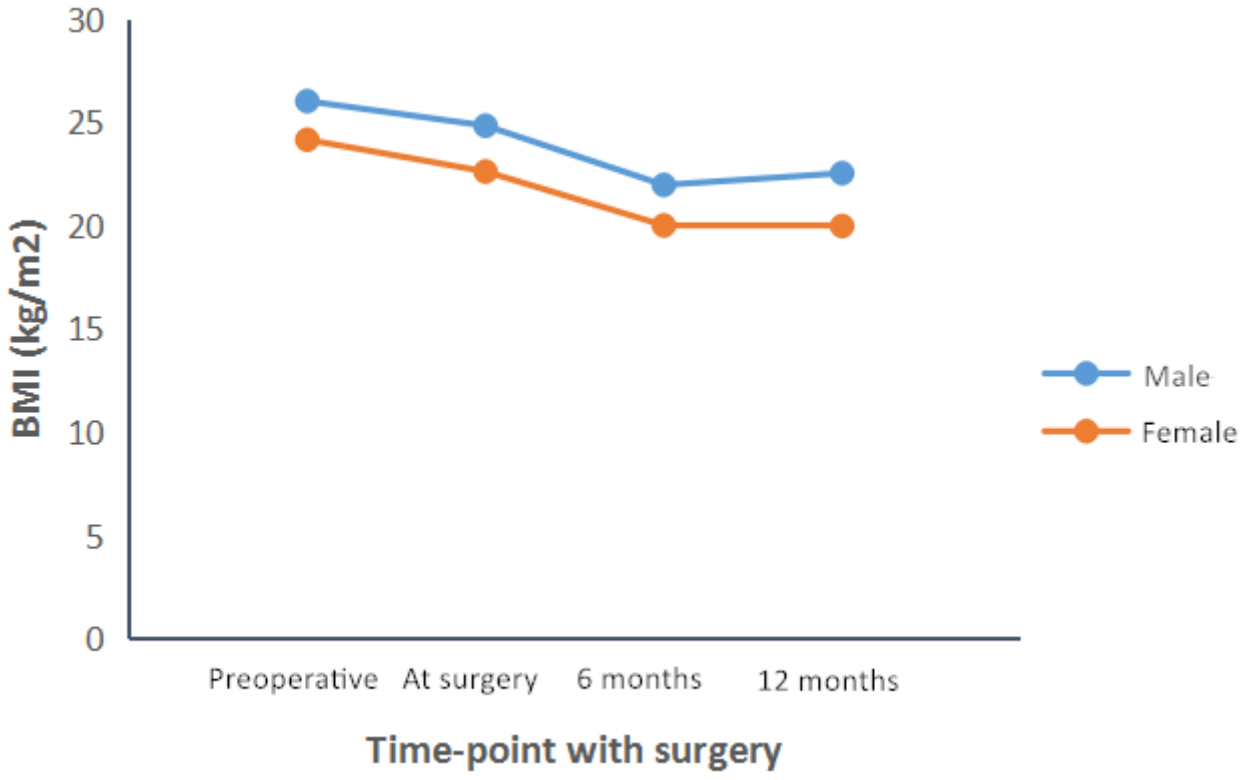
30
25
20
15
10
5
0
BMI (kg/m2)
Preoperative
At surgery
6 months
12 months
Time-point with surgery
Male
Female

Figure 2