# Original Article

# Preoperative Risk Factors and Outcomes in Esophageal Cancer Surgery - Role of Weight, Smoking, and Betel Nut Use

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## ABSTRACT

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**Background:** Esophageal cancer surgery is associated with considerable morbidity and mortality. Preoperative factors such as nutritional status, smoking, and betel nut chewing may influence postoperative outcomes but remain underexplored in this population. Aim of the study: To evaluate the impact of preoperative weight, smoking history, and betel nut use on postoperative complications and mortality in patients undergoing esophageal cancer surgery. Methods % Materials: A prospective observational study of 70 esophageal cancer patients undergoing surgery was conducted. Baseline demographics, clinical characteristics, and lifestyle habits were recorded. Postoperative complications and outcomes were analyzed. Multivariate logistic regression identified predictors of anastomotic leakage and in-hospital mortality. Result: The mean patient age was 55.5  $\pm$  10.0 years; 77.1% were male. Preoperative weight <45 kg was observed in 40%, smoking history in 47.1%, and betel nut use in 84.3%. Postoperative anastomotic leakage occurred in 12.9%, and inhospital mortality was 14.3%. Low weight (<45 kg) significantly increased the odds of anastomotic leakage (AOR 3.42, p=0.031) and mortality (AOR 3.78, p=0.048). Betel nut use was also independently associated with higher risk of leakage (AOR 5.25, p=0.040) and mortality (AOR 6.31, p=0.049). Smoking, comorbidities, and neoadjuvant therapy were not significant predictors. Conclusion: Low preoperative weight and betel nut chewing are significant predictors of postoperative complications

and mortality in esophageal cancer surgery. Addressing nutritional status and betel nut exposure preoperatively may improve surgical outcomes.

Keywords: Esophageal cancer, surgery, preoperative weight, betel nut, postoperative complications, anastomotic leakage, mortality

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#### INTRODUCTION

Esophageal cancer (EC) seriously threatens human health, and a promising new avenue for EC treatment involves cancer immunotherapy <sup>[1]</sup>. According to GLOBOCAN 2022 estimates, approximately 604,100 new cases and 544,076 deaths occurred globally, reflecting the aggressive nature and poor prognosis of this malignancy <sup>[2]</sup>. In South Asia, and particularly in Bangladesh, the burden of EC is disproportionately high <sup>[2]</sup>. Data from the World Cancer Research Fund (WCRF) indicate that, Bangladesh recorded 25,232 new cases of esophageal cancer in 2022, with an age-standardized incidence rate (ASR) of 16.0 per 100,000 population, placing it among the countries with the highest incidence rates globally <sup>[3]</sup>. Esophagectomy, the main curative approach for localized esophageal cancer, is a technically demanding surgery often accompanied by a high risk of complications and substantial postoperative challenges, even in experienced centers <sup>[4]</sup>. Therefore, identifying and addressing modifiable preoperative risk factors is critical to improving surgical outcomes. Among these, body weight (both undernutrition and obesity), cigarette smoking, and betel nut (areca nut) use are particularly relevant in South and Southeast Asia due to their high prevalence and biological impact on postoperative physiology <sup>[5]</sup>. Again, Body mass index (BMI) is a crucial determinant of perioperative risk. Undernutrition is common among EC patients due to dysphagia and cancer-induced cachexia, which may impair wound healing, reduce immune function, and increase susceptibility to infections <sup>[6]</sup>. Conversely, obesity poses challenges in surgical access and is associated with cardiopulmonary complications. Studies have shown that both low and high BMI are independently

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associated with increased postoperative complications and mortality following esophagectomy <sup>[7]</sup>. Cigarette smoking is another well-documented factor adversely affecting surgical outcomes. Smoking impairs pulmonary function, delays wound healing, and increases the risk of postoperative respiratory complications, anastomotic leaks, and overall morbidity [8]. Although smoking cessation has been shown to reduce perioperative risks, the optimal duration and timing of cessation remain areas of active investigation [9]. Betel nut chewing is deeply rooted in South Asian culture and widely practiced across Bangladesh, particularly among lower socioeconomic groups [10]. Betel nut, often combined with tobacco and slaked lime, has been classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC) [11]. While its role in carcinogenesis especially for squamous cell carcinoma of the esophagus is wellestablished, its effects on postoperative healing and complications have not been extensively studied [12]. Chronic betel use is known to cause fibrosis, vascular changes, and altered immune responses, which may impair anastomotic integrity and contribute to poor surgical outcomes [13]. Therefore, the aim of this study is to evaluate the impact of preoperative body mass index, cigarette smoking, and betel nut use on postoperative complications, in-hospital mortality, and length of hospital stay among patients undergoing curative esophagectomy for esophageal cancer in a tertiary care setting in Bangladesh.

#### **METHODS & MATERIALS**

This cross-sectional observational study was conducted in the Department of Thoracic Surgery at the National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. The study was carried out over an 18-month period, from January 2022 to June 2023. Ethical approval was obtained from the institutional review board prior to study initiation, and written informed consent was secured from all participants. A total of 70 consecutive patients were enrolled following screening for eligibility.

### **Inclusion Criteria**

- Patients of any age, sex, race, or religion
- Histologically confirmed esophageal carcinoma
- Scheduled for Ivor Lewis esophagectomy
- Provided written informed consent

#### **Exclusion Criteria**

- Known chronic kidney disease
- Concomitant malignancies
- History of previous abdominal surgery
- Declined to participate or withdrew consent

## Data Collection, Outcomes, and Surgical Protocol

Data were collected prospectively using a structured case report form and hospital records. Key demographic and clinical variables included age, sex, preoperative body weight, history of smoking (current or former), and betel nut chewing habits. Comorbid conditions such as chronic obstructive pulmonary disease (COPD), hypertension, ischemic heart

disease (IHD), and diabetes mellitus (DM) were also documented. Preoperative weight was dichotomized into <45 kg and  $\geq$ 45 kg to assess its association with outcomes. Additional variables included receipt of neoadjuvant therapy, such as chemotherapy or chemoradiotherapy. Postoperative data encompassed both clinical and biochemical outcomes. Complications such as thoracotomy wound infections, bed pneumonia, unplanned reintubation, sores, aspiration electrolyte disturbances empyema, and (notably hyponatremia and hypokalemia) were recorded. Nutritional parameters-preoperative and postoperative weight, serum total protein, and serum albumin levels-were also evaluated to assess perioperative nutritional impact. The primary outcomes were anastomotic leakage and in-hospital mortality, defined as death occurring during the index hospitalization or within 30 days postoperatively. Secondary outcomes included pulmonary and wound-related complications, electrolyte imbalances, and postoperative nutritional deterioration. The influence of weight, smoking, and betel nut use on these outcomes was specifically explored. All patients underwent an Ivor Lewis esophagectomy performed by a dedicated team of thoracic surgeons following standardized protocols. This twostage transthoracic approach included esophageal resection and gastric conduit reconstruction. Perioperative care was delivered uniformly, incorporating preoperative optimization, intraoperative hemodynamic monitoring, standardized anesthetic techniques, postoperative pain control, early mobilization, respiratory physiotherapy, and structured nutritional support. Laboratory assessments and clinical evaluations were conducted regularly to monitor postoperative recovery and detect complications promptly.

#### Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were reported as frequencies and percentages. Multivariate logistic regression was employed to identify independent predictors of anastomotic leakage and in-hospital mortality, adjusting for relevant clinical variables including low body weight, smoking history, betel nut use, comorbidities, and neoadjuvant therapy. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported. A two-tailed p-value of <0.05 was considered statistically significant.

#### RESULT

The mean age was  $55.5 \pm 10.0$  years, with most patients (45.71%) aged 50–60 years. The majority were male (77.14%). Preoperative weight was ≥45 kg in 60% of patients, with a mean of 47.6 ± 8.93 kg. Nearly half (47.14%) had a history of smoking, while betel nut use was highly prevalent (84.29%). Common comorbidities included hypertension (8.57%), diabetes mellitus (7.14%), COPD (5.71%), and ischemic heart disease (4.29%). Neoadjuvant therapy was administered in 20% of cases (Table I). Among all, the most common postoperative complications included hypokalemia (38.57%), anastomotic leakage (12.86%), and aspiration pneumonia (11.43%). Thoracotomy wound infections

occurred in 10% of patients and bed sores affected 2.86%. Other notable issues were hyponatremia (10%), combined electrolyte imbalance (10%), unplanned intubation (5.71%), and empyema (4.29%). In-hospital mortality was 14.29%, with 5.71% occurring within 7 days and 8.57% after 7 days but within 30 days. The mean hospital stay was  $14.1 \pm 5.99$  days, and the average operation time was  $319.0 \pm 40.5$  minutes (Table II). Patients experienced an average weight loss of  $2.2 \pm 6.1$  kg following esophageal cancer surgery, with mean preoperative and postoperative weights of  $47.6 \pm 8.93$  kg and  $45.4 \pm 8.59$  kg, respectively. Postoperative serum total

protein was 6.41 ± 0.83 g/dL, and serum albumin was 3.42 ± 0.37 g/dL (Table III). Multivariate logistic regression analysis revealed that patients with preoperative weight <45 kg had significantly higher odds of anastomotic leakage (AOR: 3.42, p = 0.031) and in-hospital mortality (AOR: 3.78, p = 0.048). Betel nut use was also a significant predictor of both anastomotic leakage (AOR: 5.25, p = 0.040) and in-hospital mortality (AOR: 6.31, p = 0.049). Smoking history, comorbidities, and neoadjuvant therapy were not significantly associated with either outcome (p > 0.05) (Table IV).

Variables	Frequency (n)	Percentage (%)
Age (years)		
28-40	5	7.14
40-50	15	21.43
50-60	32	45.71
60-85	18	25.71
Mean +SD	55.5±10.0	
Gender		
Male	54	77.14
Female	16	22.86
Preoperative weight		
<45 kg	28	40.00
≥45 kg	42	60.00
Mean +SD	47.6 ± 8.93	
Smoking history		
Yes	33	47.14
No	37	52.86
Betel nut chewing		
Yes	59	84.29
No	11	15.71
Comorbidity		
COPD	4	5.71
Hypertension	6	8.57
IHD	3	4.29
DM	5	7.14
Others (Hypothyroidism, old MI)	2	2.86
Received neoadjuvant therapy	14	20.00

#### Table – II: Postoperative complications and outcomes in esophageal cancer surgery (*n* = 70)

Postoperative Outcome	Frequency (n)	Percentage (%)	
Wound Complications			
Thoracotomy wound infection	7	10.00	
Bed sore	2	2.86	
Pulmonary Complications			
Aspiration pneumonia	8	11.43	
Unplanned intubation	4	5.71	
Empyema	3	4.29	
Electrolyte Imbalance			
Hypokalemia	27	38.57	
Hyponatremia	7	10.00	
Both hypoNa+K	7	10.00	
Anastomotic leakage	9	12.86	
In-hospital mortality	10	14.29	
Within 7 days	4	5.71	
After 7 days (≤30 days)	6	8.57	
Length of hospital stay, mean ± SD (days)	14.1 ± 5.99		
Operation time, mean ± SD (minutes)	319.0 ± 40.5		

Parameter	Mean ± SD (n)
Preoperative weight (kg)	47.6 ± 8.93
Postoperative weight (kg)	45.4 ± 8.59
Change in weight (kg)	$-2.2 \pm 6.1$
Postoperative serum total protein (g/dL)	$6.41 \pm 0.83$
Postoperative serum albumin (g/dL)	$3.42 \pm 0.37$

#### Table - III: Nutritional outcomes before and after surgery

#### Table – IV: Multivariate logistic regression for predictors of postoperative complications

Predictor Variable	Outcome	Adjusted Odds Ratio (AOR)	95% CI	p-value
Weight < 45 kg	Anastomotic Leakage	3.42	1.12 - 10.48	0.031*
	In-hospital Mortality	3.78	1.01 - 14.10	0.048*
Betel Nut Use	Anastomotic Leakage	5.25	1.08 - 25.55	0.040*
	In-hospital Mortality	6.31	1.01 - 39.33	0.049*
Smoking History	Anastomotic Leakage	0.71	0.19 - 2.60	0.6
	In-hospital Mortality	0.48	0.10 – 2.26	0.35
Comorbidity Present	Anastomotic Leakage	1.59	0.45 - 5.63	0.47
	In-hospital Mortality	2.11	0.54 - 8.22	0.28
Neoadjuvant Therapy	Anastomotic Leakage	0.89	0.21 - 3.72	0.87
	In-hospital Mortality	1.27	0.29 - 5.61	0.75

#### DISCUSSION

Preoperative risk factors in esophageal cancer surgery can be broadly categorized into modifiable types such as body weight, tobacco smoking, and betel nut use and nonmodifiable factors, each playing a distinct role in influencing surgical outcomes <sup>[14]</sup>. This study evaluates how demographic factors, perioperative complications, and preoperative risks particularly low body weight, smoking, and betel nut useinfluence postoperative outcomes in esophageal cancer surgery. The mean age of the study population was 55.5±10 years, with the majority of patients (45.71%) falling within the 50-60-year age range. This age distribution aligns with global data indicating the median age of esophageal cancer diagnosis typically lies between 65 and 74 years [15]. A notable male predominance (77.14%) in this cohort also reflects the recognized gender disparity in esophageal cancer incidence, which has been attributed to higher exposure to risk factors such as tobacco, alcohol, and betel nut use in men [16]. The study highlighted the high prevalence of betel nut chewing (84.29%) among patients, which was independently associated with increased odds of anastomotic leakage (AOR 5.25, p=0.040) and in-hospital mortality (AOR 6.31, p=0.049). Betel nut has been classified as a Group 1 carcinogen by the IARC and has been linked to esophageal mucosal dysplasia, fibrosis, and poor wound healing, which likely contributes to these adverse surgical outcomes <sup>[17]</sup>. This is consistent with reports from South Asia where betel nut chewing is endemic and linked with postoperative complications and poor healing <sup>[18]</sup>. Another significant finding was that patients weighing <45 kg had markedly increased risks of anastomotic leakage (AOR 3.42, p=0.031) and in-hospital mortality (AOR 3.78, p=0.048). This underscores the critical role of preoperative nutritional status in surgical outcomes, a finding mirrored by previous studies where low BMI and hypoalbuminemia were strongly correlated with increased morbidity and mortality following esophagectomy. Postoperatively, patients experienced an average weight loss of 2.2 kg and had a mean serum albumin level of 3.42 g/dL, a study on postoperative weight loss after esophagectomy reported that patients experienced a median weight loss of 12.6% within the first year after surgery, both indicative of ongoing catabolic stress and impaired nutritional recovery<sup>[19,20]</sup>. The incidence of anastomotic leakage (12.86%) and in-hospital mortality (14.29%) observed in this cohort falls within the ranges reported in global studies. For instance, Rutegård et al. noted leakage rates of 7.9% within 30 days post-surgery. Of these, 18.2% died within 90 days, compared to 6.2% mortality in patients without leakage <sup>[21]</sup>. These rates emphasize the complexity of esophageal surgery and the multifactorial nature of complications. Postoperative pulmonary complications were also notable, with aspiration pneumonia (11.43%), unplanned intubation (5.71%), and empyema (4.29%) contributing significantly to morbidity. These findings are consistent with literature where pulmonary issues remain the most common and serious postoperative problems, given the proximity of the surgical field to the airway and lung parenchyma [22]. Interestingly, neither smoking history, presence of comorbidities, nor receipt of neoadjuvant therapy were statistically significant predictors of leakage or mortality in this study. Although smoking is a well-known risk factor for esophageal malignancy, its role in postoperative outcomes remains controversial. Some studies suggest that its effects may be more pronounced in long-term recovery and pulmonary complications than in short-term mortality or leakage [23]. The mean operation time of 319  $\pm$  40.5 minutes and hospital stay of 14.1 ± 5.99 days are comparable to values reported in other surgical centers. A study on minimally invasive esophagectomy reported a mean operative time of 292 minutes and an average hospital stay of 13 days, reflecting efficient surgical performance and institutional consistency <sup>[24]</sup>. However, the relatively high incidence of electrolyte disturbances particularly hypokalemia, observed in 38.57% of cases—aligns with the findings of Wang et al., who reported an intraoperative hypokalemia rate of 49.6% in a retrospective analysis of 999 patients undergoing gastrointestinal surgery. This underscores the necessity for more vigilant perioperative electrolyte monitoring and the implementation of proactive replacement protocols to mitigate associated risks <sup>[25]</sup>. This study identifies low body weight and betel nut chewing as independent risk factors for serious postoperative complications following esophageal cancer surgery. These findings call for targeted preoperative interventions including nutritional optimization, cessation of betel nut use, and enhanced perioperative support, particularly in resource-limited settings where such risk factors are prevalent <sup>[26,27]</sup>.

#### Limitations of the study:

This study has several limitations. Being conducted at a single tertiary care center, the findings may not be generalizable to broader populations with different demographic or healthcare settings. The observational design limits causal inference between identified risk factors and postoperative outcomes. Additionally, potential recall bias in reporting smoking and betel nut habits may have influenced the accuracy of exposure data. Nutritional parameters were assessed only perioperatively, without long-term follow-up, which may underestimate the true impact of nutritional status on recovery and survival following esophageal cancer surgery.

#### **Conclusion and Recommendations**

In this cohort of esophageal cancer patients undergoing surgery, low preoperative body weight (<45 kg) and betel nut chewing were independently associated with significantly increased risks of anastomotic leakage and in-hospital mortality. These findings highlight the critical importance of assessing and optimizing nutritional status and addressing harmful habits such as betel nut use prior to surgery to improve postoperative outcomes. Smoking history, comorbidities, and neoadjuvant therapy did not demonstrate significant predictive value in this cohort. Future larger, multicenter prospective studies are warranted to validate these associations and explore targeted interventions to mitigate risk.

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