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Original Article

Factors Affecting Hospital Morbidity and Mortality after Esophageal Resection for Esophageal Carcinoma

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ABSTRACT

Background: Since its introduction, esophageal resection has been notable for high rates of morbidity and mortality. Despite many retrospective reviews, conclusions regarding which patients may be at undue risk for complications are difficult to infer. Aim of this study was to evaluate the preoperative and postoperative factors affecting the hospital morbidity and mortality following esophageal resection for esophageal carcinoma. The study has been performed to standardize the criteria of patient selection and intensive postoperative care for patients undergoing esophageal surgery for esophageal carcinoma.

Methods: It is a descriptive longitudinal study, performed in department of thoracic surgery, Dhaka Medical College Hospital from 1st July 2015 to 30th June 2016. Total 50 cases were included in this study. Purposive sampling was done and surgical intervention was carried out by surgeons ranked assistant professor or above.

Results: Of the 50 collected cases, mean age was 52.10 (±14.69) years with minimum age of 32 and maximum, 80 years. 78% were male and 22% female. 28 (56%) patients underwent one stage esophageal resection for esophageal carcinoma and 22 (44%) patients underwent two stage esophageal resection. Out of 50 patients undergoing esophageal resection, complications occurred in 52% of patients leading to postoperative morbidity, 10% patients died following surgery during hospital stay and uneventful recovery occurred in 38% of patients. Respiratory complication was the leading cause of hospital morbidity (42.30%) following esophageal resection with predominance (30.77%) among stage III patients. Mortality rates were 5.26% in stage I patients, 11.11% in stage II patients and 15.38% in stage III patients. Comparison among different classes of ASA (American Society of Anaesthesiologists) score revealed better post operative outcome in patients with Class I and poor results in Class III patients. Post operative mortality rates of age group 61 to 70 and 71 to 80 were 33.33% and 50% respectively compared to 00.0% in 31-40 age group. Outcome of patients with squamous cell carcinoma and adenocarcinoma were quite similar.

Conclusion: This study showed that respiratory complication was the leading cause of hospital morbidity and mortality following esophageal resection for esophageal carcinoma. Old age, poor lung function test results, high ASA score and stage III disease have been found to be associated with poor post operative outcome after esophageal resection.

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Introduction

Cancer of the esophagus is the sixth leading cause of cancer death worldwide. Most of these tumors are of squamous cell origin and are located in the middle and lower thirds of the esophagus. Moreover, the incidence of adenocarcinoma of the distal esophagus and gastroesophageal junction is increasing more rapidly than that of any other solid tumor. Advanced stage of disease is seen at presentation in more than 75% of the patients. Despite advances in the various therapeutic modalities, surgery has remained the mainstay of treatment for patients with potentially

resectable esophageal cancer. Five-year survival rates as high as 30% to 40% have been reported after curative resection in some centers. ^{3,4}

Esophageal resection is the mainstay of therapy for malignancy of the esophagus and gastroesophageal junction.⁵ However, it is associated with considerable morbidity and mortality. While advances in perioperative management strategies have improved early morbidity, complications of esophageal resection continue to be appreciably higher than other similarly complex operations such as pancreatectomy, gastrectomy, and hepatectomy. ^{6, 7, 8} Furthermore, as the average 5-year survival for esophageal cancer patients is still only 25%, ⁹ the impact of surgical complications on quality of life cannot be overstated, particularly when the consideration of limited life expectancy exists. ^{10, 11}

Most tumours are excised using the Lewis-Tanner approach, where a separate upper abdominal incision and right sided postero-lateral thoracotomy are used for resection. This procedure is performed mainly for tumours of the middle and lower third of the esophagus. A three phase esophagectomy is indicated for upper third tumours. When a tumour encroaches on the gastroesophageal junction, a proximal gastric resection is carried out as part of an esophagogastrectomy, which is a single stage operation. ¹²

In the past 2 decades, advances in noninvasive imaging, preoperative staging, and anesthesia specially single lung ventilation, combined with refinements in surgical technique, postoperative care, and adjuvant therapy, have enabled experienced centers to reduce postoperative mortality rates and enhance complete resection. ^{13, 14} However, that has failed to translate more often into any significant benefit in hospital morbidity and mortality. In selected centers and in subgroups of patients who underwent radical esophagectomy, 5-year survival rates of 40% or above could be achieved. ¹⁵⁻²⁰

Surgery is traditionally viewed as the most effective way to ensure both locoregional control and long-term survival. Therefore, use of radical surgical procedures, is considered reasonable to improve overall outcome.²¹ To have any impact on long-term survival in these patients, it is essential to minimize postoperative mortality and morbidity by improved patient selection, optimizing surgical technique and perioperative care.²²

Moreover, patients with high risk of incomplete surgical resection, recurrent disease, or cancer-related death must be identified to propose them nonsurgical treatment.^{23, 24}

Despite advances in the management of patients with esophageal cancer, esophagectomy remains an operation with relatively high morbidity and mortality. Important post-esophagectomy complications are categorized traditionally into two groups: medical and surgical. The most commonly reported medical causes of death and morbidity have been pulmonary complications (pneumonia, respiratory failure, pleural effusion). Different cardiac complications (myocardial infarction, heart failure, arrhythmia) also contribute to post-operative morbidity and death. Recorded imminent surgical complications are- anastomotic leakage, wound infection, septicaemia, stricture formation and recurrence. ²⁵⁻³⁰

To date, various studied have been carried out to identify and address different pre-operative risk factors for esophageal resection. Increasing age, poor swallowing scores, high ASA score, stage of tumour, impaired lung function test, tobacco use and surgery in patients with other co-morbidities have been associated with poor surgical outcomes in these studies. Esophagectomy procedure has also been a major predictive factor affecting surgical outcome. ²⁵⁻²⁹ Respiratory complications and anastomotic leakage are two most important predictors of post-operative mortality. ³⁰

The aim of this study is to evaluate the preoperative and postoperative factors affecting the morbidity and mortality following esophageal resection for esophageal carcinoma. Multiple preoperative and postoperative factors will be assessed. In spite of many limitations, the purpose of selecting this topic is to make an effort in eliciting detailed information regarding factors influencing mortality and morbidity for patients of esophageal carcinoma undergoing esophageal resection.

Materials and Methods

The study was designed as a prospective study and carried out from July, 2015 to June, 2016 at department of Thoracic Surgery in Dhaka Medical College Hospital. Total number of 50 cases were included in this study by using consecutive sampling technique.

Following patient's admission, operable cases of esophageal carcinoma were identified and patients' demographic characteristics, histopathological diagnosis and preoperative investigations were recorded. On the basis of the report of endoscopist, tumour location was identified. Patients were sent to department of anaesthesiology for pre-anaesthetic check up and ASA scoring.

Esophageal resections were carried out under general anaesthesia with single lung ventilation. Two- stage procedure or Ivor-Lewis procedure was done for middle third tumour and single stage procedure or Sweet's procedure for lower-third tumour. Meticulous and documented post-operative follow-up was ensured, and mortality and morbidity assessment were done in terms of different pre and post-operative variables. Then comparisons among different outcomes were established. Structured questionnaire and data sheet were used to collect data. After editing and coding, the coded data was analyzed by computer with the help of SPSS software.

Results

The mean age of the study population was 52.10(±14.69) years. Minimum age was 32 years and maximum age, 80 years. Of the study population, 78% were male and 22% female. Considering location of tumor, 44% (n=22) of patients had esophageal carcinoma in the middle part undergoing two stage esophageal resection and 56% (n=28) in lower third undergoing one stage esophageal resection. Slight majority (52%) were squamous cell carcinoma of different grades and 48% were adenocarcinoma of different grades. Among the patients of different stages, 38% were at stage I, 36% at stage II and 26% were at stage III. Most of the adenocarcinoma patients were at stage I (41.67%). Squmous cell carcinoma patients were mostly at stage I and II (34.62% each).

Regarding common TNM staging of post-esophagectomy specimen of the study population, T2 disease was 56% followed by T3, 30%. Considering nodal status most of the cases were N0, 54% with N1, 32% and N2, 14%. All the cases were at M0 stage. Most of the patients undergoing esophageal resection had class I ASA score (62%). Next in percentage frequency was Class II (28%). There were no patients of Class IV or V ASA score.

Out of 50 patients undergoing esophageal resection, complications occurred in 52% of patients leading to

postoperative morbidity, 10% patients died following surgery during hospital stay and uneventful recovery occurred in 38% of patients. Respiratory complication was the leading cause of hospital morbidity (42.30%) following esophageal resection with predominance (30.77%) among stage III patients. Pneumonia was the most important respiratory complications affecting 54.54% of patients. Mortality rates were 5.26% in stage I patients, 11.11% in stage II patients and 15.38% in stage III patients. Comparison among different classes of ASA score revealed better post operative outcome in patients with Class I and poor results in Class III patients. Post operative mortality rates of age group 61 to 70 and 71 to 80 were 33.33% and 50% respectively compared to 00.0% in 31-40 age group.

Following one stage esophageal resection post operative complications were 50.00% and mortality rate was 7.14%. Rates were 54.54% and 13.67% in case of two stage operation. Outcome of patients with squamous cell carcinoma (12 developed complications, 02 died) and adenocarcinoma (14 developed complications, 3 died) were quite similar.

Table 1. Outcome of patients following esophageal resection (n=50)

Outcome	Number of Patients	Percentage frequency (%)
Uneventful recovery	19	38.0
Morbidity	26	52.0
Death	05	10.0
Total	50	100.0

Table 2. Morbidity and mortality of patients from different complications

Complications	Morbidity	Death	
	N	N	
Respiratory	11 (42.30%)	02 (40.0%)	
Cardiac	01 (03.84%)	00 (00.0%)	
Wound infection	07 (26.92%)	00 (00.0%)	
Anastomotic leak	05 (19.23%)	03 (60.0%)	
Others	02 (07.69%)	00 (00.0%)	
Total	26 (100.0%)	05 (100.0%)	

N : Number of patients with esophageal resection in the study population.

P : Percentage of patients with esophageal resection in the study population.

Percentage figures are given in parentheses.

Outcome	Stage I	Stage II	Stage III
	N	N	N
Uneventful recovery	09 (47.36%)	07 (38.89%) 03 (23.07%)	
Respiratory complications	03 (15.78%)	04 (22.22%)	04 (30.77%)
Cardiac complications	01 (05.26%)	00 (00.0%)	00 (00.0%)
Wound infection	03 (15.78%)	02 (11.11%)	02 (15.38%)
Anastomotic leak	00 (00.0%)	03 (16.67%)	02 (15.38%)
Others	02 (10.52%)	00 (00.0%)	00 (00.0%)
Death	01 (05.26%)	02 (11.11%)	02 (15.38%)
Total	19 (100.0%)	18 (100.0%)	13 (100.0%)

N : Number of patients with esophageal resection in the study population.

Percentage figures are given in parentheses.

Table 4. Respiratory complications and death in patients with variable lung function test findings

Lung function test findings	Respiratory complications	Death	
	N	N	
Normal (n=30)	03 (10.0%)	00 (00.0%)	
Mild abnormality (n=12)	03 (25.0%)	00 (00.0%)	
Moderate abnormality (n=07)	04 (57.14%)	01 (14.28%)	
Severe abnormality (n=01)	01 (100.0%)	01 (100.0%)	

n : Number of patients with specific lung function test findings.

Percentage figures are given in parentheses.

Table 5. Outcome of patients with different ASA score (n=50)

Outcome	Class I	Class II	Class III
	N	N	N
Uneventful recovery	16 (55.17%)	03 (21.43%)	00 (00.0%)
Respiratory complications	05 (17.24%)	04 (28.57%)	02 (28.57%)
Cardiac complications	01 (3.45%)	00 (00.0%)	00 (00.0%)
Wound infection	03 (10.34%)	03 (21.43%)	01 (14.28%)
Anastomotic leak	01 (3.45%)	02 (14.28%)	02 (28.57%)
Other complications	02 (6.90%)	00 (00.0%)	00 (00.0%)
Death	01 (3.45%)	02 (14.28%)	02 (28.57%)
Total	29 (100.0%)	14 (100.0%)	07 (100.0%)

N : Number of patients with esophageal resection in the study population.

Percentage figures are given in parentheses.

P: Percentage of patients with esophageal resection in the study population.

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Age	Uneventful recovery N	Complications N	Death N	Total
31-40	05 (83.33%)	01 (16.67%)	00 (00.0%)	06 (100.0%)
41-50	05 (33.33%)	09 (60.00%)	01 (6.67%)	15 (100.0%)
51-60	07 (33.33%)	13 (61.90%)	01 (4.76%)	21 (100.0%)
61-70	02 (33.33%)	02 (33.33%)	02 (33.33%)	06 (100.0%)
71-80	00 (00.0%)	01 (50.0%)	01 (50.0%)	02 (100.0%)

N: Number of patients with esophageal resection in the study population.

Percentage figures are given in parentheses.

Discussion

The present study is planned to assess the factors affecting short term outcome after esophageal resection for esophageal carcinoma. Specific objectives were to determine the factors influencing survival and rates of death and complications after esophageal resection, evaluate the preoperative factors in treating operable cases of esophageal carcinoma and standardize an ideal work up module for improved patient selection and meticulous perioperative care in patients undergoing esophageal resection for esophageal carcinoma.

This study states that following esophageal resection, uneventful recovery occurred in 38% of patients and morbidity due to various complications were observed in 52% of patients. Post operative mortality rate was 10%. Post operative hospital death rate of this study was consistent with studies of Brian P. Whooley *et al* and Mark K. Ferguson *et al* Brian P. Whooley *et al* found 11% hospital death following esophageal resection and Mark K. Ferguson *et al*²⁵ observed 12% hospital mortality. On the contrary, B. Zane Atkins *et al*³¹ showed 5.8% post operative mortality and similar result was found in Christophe Mariette *et al*³² study. Study conducted by B. Zane Atkins *et al*³¹ showed 64% post operative morbidity which was almost similar to what was found in this study.

In this study, post-operative complications were found in 26 patients. Respiratory complications were present in 42.30% of patients, cardiac complications in 3.84%, anastomotic leak in 19.23% and wound infection in 26.92% of patients. Mark K. Ferguson *et al*²⁵ and Christopher E Avendano *et al*³³ found 38% and 36.1% pulmonary complications respectively which are consistent with this study. Moreover, study

by Cameron D. Wright et al34 showed 2% cardiac morbidity and B. Zane Atkins et al32 showed 14% anastomotic leak following esophagectomy which are almost similar with this study. Considering different respiratory complications following esophageal resection, pneumonia were found in 54.54% of patients, atelectasis in 18.18% and respiratory failure in 27.28% of patients. Results were partially supported by study conducted by Guillaume Taillier et al³² which showed pneumonia in 55%, respiratory failure in 32% and atelectasis in 12.5% of patients suffering from respiratory complications following esophagectomy. Reviewing the study results, it was obvious that among different types of wound infection superficial surgical site infection occurred in 28.57% of patients, deep surgical site infection in 57.14% of patients and 14.2% of patients developed complete wound dehiscence. There is no pertinent and reliable data or study to support or deny this result except a study by B. Zane Atkins et al³² which showed that among 379 patients undergoing esophageal resection 11.9% of patients (45 in number) developed wound infection and 2.1% of patients (8 in number) developed complete wound dehiscence.

Study revealed that post-operative morbidity and mortality rates were high in stage II and stage III esophageal carcinoma patients who underwent esophageal resection. Uneventful recovery occurred in 47.36% patients of stage I and 23.07% of patients with stage III. Mortality rates were 05.26%, 11.11% and 15.38% respectively in stage I, II and III diseases undergoing esophageal surgery. Same results were found in Cameron D. Wright *et a* 34 where mortality rates were 5.8%, 13% and 18% in stage I, II and III diseases. Regarding pre-operative lung function test

P: Percentage of patients with esophageal resection in the study population.

affecting post-operative outcome, it is noted that respiratory complications and mortality rates were higher in patients of moderate to severe restrictive abnormality. Respiratory complications in normal lung function test and mildly abnormal lung function test patients were 10% and 25% respectively. Figures were 57.14% and 100% in patients of moderate and severe restrictive abnormalities. According to Cameron D. Wright *et al*³⁴ respiratory complications were 36%, 33% and 22.3% respectively in patients of normal lung function, mild restrictive abnormality and severely impaired lung function. Amy D. Celauro *et al*²⁵ also established in their study that lung function is an independent predictor of respiratory complications and post-operative hospital mortality.

Observations regarding ASA score affecting outcome after surgery demonstrates that post operative morbidity and mortality was higher in class III patients in comparison to class I. Mortality rate was 28.57%, 14.28% and 3.45% respectively in class III, class II and class I patients. There was significant difference in complications between class I and class III patients. This was also supported by study of Cameron D. Wright et al34 which stated 26.9%, 18.2% and 14.1% postoperative mortality and morbidity respectively in class III, class II and class I patients. Hospital death rates were maximum in 71 to 80 years age group accounting about 50.0%, followed by 61-70 years age group-33.33%. This rate was nil in 31-40 years age group. This result was consistent with other studies. John C. Kucharczuk et al34 found 55.5% of post-operative mortality in 71-80 years age group, 46% in 61-70 age group and less than 5% mortality in less than 60 years age group. Unlike post-operative mortality, postoperative complications were found not to be associated with increasing age in this study, which was supported by study of Mark K. Ferguson et al.25 Future studies are needed to focus in greater detail on the preoperative risk factors such as smoking, body mass index, co-morbidities, serum albumin level, perioperative blood transfusion etc. which may affect the magnitude of postoperative complications following esophageal resection. Large scale multicentre study should be conducted to conclude over this common and burning issue.

Conclusion

The results of the present study demonstrates that old age, poor lung function test results, high ASA scores and stage III diseases are associated with poor

post operative outcome after esophageal resection. Respiratory complication is the leading cause of hospital morbidity and mortality following esophageal resection for esophageal carcinoma. Proper assessment of certain factors can immensely improve the prognosis following esophageal resection for esophageal carcinoma.

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