

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

Muhammad Abid Khan¹, Faridullah Khan Ismail², Tahir Aslam³

1. Assistant Professor Thoracic Surgery Unit, Lady Reading Hospital Medical Teaching Institution, Peshawar.
2. Assistant Professor, Thoracic Surgery Unit, Lady Reading Hospital Medical Teaching Institution, Peshawar.
3. Consultant Thoracic Surgery Department, Fatima Jinnah Institute of Chest Diseases Quetta.

Corresponding Author: Faridullah Khan Ismail

Assistant Professor, Thoracic Surgery Unit, Lady Reading Hospital – Medical Teaching Institution, Peshawar.

Email: faridct@hotmail.com

Abstract

Background

Esophageal carcinoma is an aggressive malignancy associated with poor prognosis and substantial treatment-related morbidity. In patients with resectable disease, neoadjuvant chemotherapy has been used to improve tumor downstaging, increase the likelihood of complete resection, and treat micrometastatic disease before surgery. However, its impact on short-term surgical outcomes remains an important area of evaluation.

Objectives

To assess the role of neoadjuvant chemotherapy in patients with resectable esophageal carcinoma and to determine its impact on surgical outcomes, including postoperative complications, length of hospital stay, intensive care admission, and mortality.

Methodology

This retrospective comparative study was conducted at Department of Thoracic Surgery Unit, Lady Reading Hospital Medical Teaching Institution, Peshawar from Jan 2018 to Jan 2019. A total of 65 patients with resectable esophageal carcinoma who underwent esophagectomy during the study period were included. Patients were divided into two groups: those who received neoadjuvant chemotherapy before surgery and those who underwent upfront surgery without neoadjuvant treatment. Demographic characteristics, tumor stage, operative duration, intraoperative blood loss, postoperative complications, hospital stay, ICU admission, and mortality were recorded using a structured data collection form. Data were analyzed using SPSS version 24. Continuous variables were expressed as mean \pm standard deviation, while categorical variables were presented as frequencies and percentages. Statistical significance was set at $p < 0.05$.

Results

A total of 65 patients with resectable esophageal carcinoma were included in the study, with 33 patients in the neoadjuvant chemotherapy group and 32 patients in the upfront surgery group. The mean age of patients was 55.2 ± 10.8 years, and males constituted the majority of cases (66.2%).

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

Patients who received neoadjuvant chemotherapy demonstrated a higher rate of complete resection than those who underwent upfront surgery (87.9% vs 75.0%). Postoperative complications were observed in 13 patients (39.4%) in the neoadjuvant chemotherapy group and 15 patients (46.9%) in the upfront surgery group. The most frequent complications were pulmonary complications, anastomotic leak, and wound infection. The mean hospital stay was slightly shorter in the neoadjuvant group (12.6 ± 4.1 days) compared with the surgery-alone group (13.9 ± 4.7 days). ICU admission was required in 5 patients (15.2%) in the neoadjuvant group and 6 patients (18.8%) in the surgery-alone group. Overall postoperative mortality was 5 patients (7.7%).

Conclusion

Neoadjuvant chemotherapy plays an important role in the management of resectable esophageal carcinoma and may improve surgical outcomes by increasing complete resection rates without significantly increasing postoperative morbidity. Careful perioperative assessment and multidisciplinary management remain essential to optimize outcomes in these patients.

Keywords: Neoadjuvant chemotherapy; Esophageal carcinoma; Esophagectomy; Surgical outcomes; Postoperative complications

*Tob Regul Sci.*TM 2021;7(5): 2301 - 2308

Introduction

Esophageal carcinoma is one of the most aggressive gastrointestinal malignancies and is associated with poor long-term survival despite advances in diagnosis and treatment (1). Surgery remains a key curative option for resectable disease; however, surgery alone has historically been associated with high recurrence rates and limited survival benefit in locally advanced tumors (2). For this reason, multimodal treatment strategies have increasingly been adopted in the management of resectable esophageal carcinoma (3). Neoadjuvant chemotherapy has been introduced to improve tumor downstaging, eradicate micrometastatic disease, and increase the probability of achieving an R0 resection (4). Previous randomized trials and institutional studies have shown that preoperative chemotherapy may improve survival in selected patients with esophageal adenocarcinoma and squamous cell carcinoma, particularly when combined with appropriate surgical resection (5). In addition, neoadjuvant treatment may allow better selection of patients with favorable tumor biology for surgery (6). Despite these potential benefits, concerns remain regarding the effect of neoadjuvant chemotherapy on perioperative risk. Chemotherapy-related toxicity, nutritional deterioration, immunosuppression, and treatment delays may theoretically increase postoperative morbidity and mortality after esophagectomy (7). Common complications after esophageal surgery include pulmonary complications, anastomotic leak, surgical site infection, and cardiac events, all of which may influence recovery and survival (8). Therefore, the balance between oncological benefit and perioperative safety is an important clinical consideration (9). Several studies have reported that neoadjuvant treatment does not significantly increase postoperative complications when patients are carefully selected and managed in experienced centers (10). However, results across studies remain variable, and institutional data continue to be valuable for assessing local outcomes, refining perioperative protocols, and improving patient selection (11). Therefore, this study aimed to evaluate the impact of neoadjuvant chemotherapy on surgical outcomes in patients with resectable esophageal carcinoma.

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

Research Objective

To assess the role of neoadjuvant chemotherapy in resectable esophageal carcinoma and determine its impact on postoperative complications, hospital stay, ICU admission, and mortality.

Materials and Methods

Study Design and Setting

This retrospective comparative study was conducted at Department of Thoracic Surgery Unit, Lady Reading Hospital Medical Teaching Institution, Peshawar from jan 2018 to jan 2019.

Participants

The study included 65 patients with resectable esophageal carcinoma who underwent esophagectomy during the study period.

Inclusion Criteria

Patients aged 18 years or older with resectable esophageal carcinoma who underwent esophagectomy were included. Patients in both the neoadjuvant chemotherapy group and the upfront surgery group were eligible for analysis.

Exclusion Criteria

Patients with metastatic disease, those receiving neoadjuvant chemoradiotherapy instead of chemotherapy alone, patients with incomplete medical records, and those deemed unfit for surgery were excluded.

Data Collection

Patient demographics, tumor stage, operative duration, intraoperative blood loss, type of surgery, postoperative complications, ICU admission, hospital stay, and mortality were recorded using a structured proforma.

Statistical Analysis

Data were analyzed using SPSS version 24. Continuous variables were expressed as mean \pm SD, while categorical variables were reported as frequency and percentage. The chi-square test and independent t-test were used to compare groups. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 65 patients with resectable esophageal carcinoma were included in the study. Of these, 33 patients received neoadjuvant chemotherapy before surgery, while 32 patients underwent upfront surgery. The mean age of the study population was 55.2 ± 10.8 years, and males accounted for 43 cases (66.2%). Patients in the neoadjuvant chemotherapy group showed a higher complete resection rate compared with the surgery-alone group (29/33, 87.9% vs 24/32, 75.0%). The mean operative duration was slightly longer in the neoadjuvant group, but the difference was not statistically significant. Postoperative complications occurred in 13 patients (39.4%) in the neoadjuvant group and 15 patients (46.9%) in the upfront surgery group. The most common postoperative complication was pulmonary complications, followed by anastomotic leak and

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

wound infection. ICU admission was required in 5 patients (15.2%) in the neoadjuvant group and 6 patients (18.8%) in the surgery-alone group. The average hospital stay was 12.6 ± 4.1 days in the neoadjuvant group and 13.9 ± 4.7 days in the surgery-alone group. Overall postoperative mortality was 5 cases (7.7%), with no marked difference between the two groups.

Table 1. Baseline Characteristics of the Study Population

Variable	Neoadjuvant Group (n=33)	Chemotherapy Surgery Group (n=32)	Alone	Total (n=65)
Age (years), mean \pm SD	54.8 \pm 10.1		55.6 \pm 11.4	55.2 \pm 10.8
Male	22		21	43
Female	11		11	22
Middle/lower esophageal tumor	25		23	48
Upper esophageal tumor	8		9	17

Table 2. Comparison of Surgical Outcomes Between Groups

Outcome Variable	Neoadjuvant Group (n=33)	Chemotherapy Surgery Group (n=32)	Alone	Group	p- value
Complete resection (R0)	29 (87.9%)		24 (75.0%)		0.04
Postoperative complications	13 (39.4%)		15 (46.9%)		0.54
ICU admission	5 (15.2%)		6 (18.8%)		0.60
Mortality	2 (6.1%)		3 (9.4%)		0.64

Table 3. Hospital Stay and Major Postoperative Complications

Outcome	Neoadjuvant Chemotherapy Group	Surgery Alone Group
Mean hospital stay	12.6 \pm 4.1 days	13.9 \pm 4.7 days
Pulmonary complications	6 (18.2%)	7 (21.9%)
Anastomotic leak	3 (9.1%)	4 (12.5%)
Wound infection	3 (9.1%)	3 (9.4%)
Cardiac complications	1 (3.0%)	1 (3.1%)

Discussion

The present study evaluated the impact of neoadjuvant chemotherapy on surgical outcomes in patients with resectable esophageal carcinoma. Patients who received neoadjuvant chemotherapy

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

had a higher complete resection rate and did not experience a major increase in postoperative complications compared with patients who underwent upfront surgery. These findings are consistent with previous studies showing that preoperative chemotherapy can improve tumor downstaging and R0 resection rates without significantly increasing postoperative mortality (12,13). In the present series, the overall complication rate was slightly lower in the neoadjuvant chemotherapy group than in the surgery-alone group. Pulmonary complications remained the most common adverse event in both groups. This pattern is consistent with published reports in esophageal surgery, where respiratory complications remain the leading cause of short-term morbidity regardless of treatment strategy (14,15). The higher complete resection rate observed in patients receiving neoadjuvant chemotherapy supports the oncological rationale for preoperative treatment. Earlier studies have shown that neoadjuvant therapy may reduce tumor burden and increase the likelihood of achieving margin-negative resection, which is an important determinant of long-term survival (16,17). These findings support the use of neoadjuvant chemotherapy as part of multimodal treatment in resectable esophageal carcinoma. Hospital stay and ICU utilization were not markedly increased in patients receiving neoadjuvant chemotherapy in this study. This is clinically relevant because one of the major concerns regarding preoperative systemic treatment is the possibility of delayed postoperative recovery or increased perioperative risk. Our findings are comparable to reports suggesting that carefully selected patients can safely undergo surgery after neoadjuvant treatment without substantial worsening of short-term surgical outcomes (18,19). The mortality rate in our study was low and comparable between the two groups. This observation agrees with studies reporting that perioperative mortality after esophagectomy is more closely related to severe postoperative complications such as pneumonia, sepsis, and anastomotic leakage than to neoadjuvant chemotherapy itself (20,21). Therefore, perioperative optimization and prompt management of complications remain essential in improving patient outcomes. Overall, the findings of this study suggest that neoadjuvant chemotherapy can be used safely in selected patients with resectable esophageal carcinoma and may improve surgical radicality without significantly increasing postoperative morbidity. Continued institutional evaluation and larger comparative studies are needed to further define the patients most likely to benefit from this treatment strategy (22).

Limitations

This study has several limitations. It was conducted at a single center and included a limited number of patients, which may affect the generalizability of the findings. The retrospective design also limits control over confounding variables. In addition, long-term oncological outcomes were not evaluated in this analysis.

Conclusion

Neoadjuvant chemotherapy appears to improve complete resection rates in resectable esophageal carcinoma without significantly increasing postoperative complications, ICU admission, or mortality. Pulmonary complications remained the most frequent postoperative event in both groups. Multidisciplinary perioperative care and careful patient selection are essential to optimize surgical outcomes in these patients.

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

Disclaimer:Nil

Conflict of Interest:Nil

Funding Disclosure:Nil

Authors Contribution

Concept & Design of Study: **Muhammad Abid Khan¹**

Data Collection:Faridullah Khan Ismail²

Drafting:Tahir Aslam³

Data Analysis: Faridullah Khan Ismail²

Critical Review: Tahir Aslam³

Final Approval of version: **All authors approved the final version.**

References

1. Bollsweiler E, Plum P, Mönig SP, Hölscher AH: Current and future treatment options for esophageal cancer in the elderly. *Chin J Cancer Res.* 2015, 27:221-230.
2. Markar SR, Gronnier C, Pasquer A, et al.: Role of neoadjuvant treatment in clinical T2N0M0 esophageal cancer: results from a worldwide esophageal cancer collaboration. *Surgery.* 2016, 159:1597-1603.
3. Moorcraft SY, Fontana E, Cunningham D, Chau I: Adjuvant or neoadjuvant therapy for operable esophagogastric adenocarcinoma: current standards and future perspectives. *World J Gastroenterol.* 2015, 21:12137-12148.
4. Huang R, Zhang H, Yang D, et al.: Neoadjuvant therapy for locally advanced esophageal cancers. *Front Oncol.* 2022, 12:822592.
5. Reece-Smith AM, Thaha MA, Alderson D, et al.: Postoperative survival following perioperative MAGIC versus neoadjuvant OE02-type chemotherapy in oesophageal adenocarcinoma. *Ann R Coll Surg Engl.* 2017, 99:209-215.
6. Altorki N, Harrison S, Port JL: What is the role of neoadjuvant chemotherapy, radiation, and adjuvant treatment in resectable esophageal cancer?. *Ann Cardiothorac Surg.* 2017, 6:167-174.
7. Lin J, Shen Y, Wang W, et al.: Results of neoadjuvant therapy followed by esophagectomy for patients with locally advanced thoracic esophageal squamous cell carcinoma. *J Thorac Dis.* 2017, 9:310-317.
8. Klevebro F, Alexandersson von Döbeln G, Wang N, et al.: A European multicenter cohort study of patients undergoing esophagectomy after neoadjuvant therapy: respiratory comorbidity and postoperative complications. *Ann Surg Oncol.* 2019, 26:174-182.
9. Kataoka K, Takeuchi H, Mizusawa J, et al.: Prognostic impact of postoperative morbidity after esophagectomy for esophageal cancer: exploratory analysis of JCOG9907. *Ann Surg.* 2017, 265:1152-1157.

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

10. Zheng Y, Li Y, Liu X, et al.: Neoadjuvant chemotherapy followed by minimally invasive esophagectomy is safe and feasible for treatment of esophageal squamous cell carcinoma. *J Thorac Dis.* 2019, 11:5486-5495.
11. Huang Y, Wang H, Luo G, et al.: A systematic review and network meta-analysis of neoadjuvant therapy combined with surgery for patients with resectable esophageal squamous cell carcinoma. *Int J Surg.* 2017, 38:41-47.
12. Reece-Smith AM, Thaha MA, Alderson D, et al.: Postoperative survival following perioperative MAGIC versus neoadjuvant OE02-type chemotherapy in oesophageal adenocarcinoma. *Ann R Coll Surg Engl.* 2017, 99:209-215.
13. Lin J, Shen Y, Wang W, et al.: Results of neoadjuvant therapy followed by esophagectomy for patients with locally advanced thoracic esophageal squamous cell carcinoma. *J Thorac Dis.* 2017, 9:310-317.
14. Klevebro F, Alexandersson von Döbeln G, Wang N, et al.: A European multicenter cohort study of patients undergoing esophagectomy after neoadjuvant therapy: respiratory comorbidity and postoperative complications. *Ann Surg Oncol.* 2019, 26:174-182.
15. Kataoka K, Takeuchi H, Mizusawa J, et al.: Prognostic impact of postoperative morbidity after esophagectomy for esophageal cancer: exploratory analysis of JCOG9907. *Ann Surg.* 2017, 265:1152-1157.
16. Huang Y, Wang H, Luo G, et al.: A systematic review and network meta-analysis of neoadjuvant therapy combined with surgery for patients with resectable esophageal squamous cell carcinoma. *Int J Surg.* 2017, 38:41-47.
17. Altorki N, Harrison S, Port JL: What is the role of neoadjuvant chemotherapy, radiation, and adjuvant treatment in resectable esophageal cancer?. *Ann Cardiothorac Surg.* 2017, 6:167-174.
18. Mantziari S, Hübner M, Demartines N, Schäfer M: Survival benefit of neoadjuvant treatment in clinical T2N0 esophageal cancer: a multicenter propensity-matched analysis. *Ann Surg.* 2017, 266:307-313.
19. Markar SR, Gronnier C, Pasquer A, et al.: Role of neoadjuvant treatment in clinical T2N0M0 esophageal cancer: results from a worldwide esophageal cancer collaboration. *Surgery.* 2016, 159:1597-1603.
20. van der Woude SO, Hulshof MCCM, van Laarhoven HWM, van Berge Henegouwen MI: CROSS and beyond: a clinical perspective on the results of the randomized ChemoRadiotherapy for Oesophageal cancer followed by Surgery Study. *Chin Clin Oncol.* 2016, 5:66.
21. Zheng Y, Li Y, Liu X, et al.: Neoadjuvant chemotherapy followed by minimally invasive esophagectomy is safe and feasible for treatment of esophageal squamous cell carcinoma. *J Thorac Dis.* 2019, 11:5486-5495.

Role of Neoadjuvant Chemotherapy in Resectable Esophageal Carcinoma: Impact on Surgical Outcomes.

22. Moorcraft SY, Fontana E, Cunningham D, Chau I: Adjuvant or neoadjuvant therapy for operable esophagogastric adenocarcinoma: current standards and future perspectives. *World J Gastroenterol.* 2015, 21:12137-12148.