

ORIGINAL ARTICLE

Long-Term Survival and Toxicity in Medically Inoperable Carcinoma Esophagus Following Induction Chemotherapy and Concurrent Chemoradiation in a Tertiary Care Setting

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ABSTRACT

Background: Carcinoma of the esophagus, particularly middle one-third, presents unique treatment challenges. This study evaluates long-term survival outcomes and treatment-related toxicity in patients with medically inoperable esophageal carcinoma treated with induction chemotherapy followed by concurrent chemoradiation.

Methods: A retrospective analysis was conducted at a tertiary care hospital on patients diagnosed with carcinoma esophagus (middle one-third) from 2015 to 2020. Patients were selected based on medical inoperability and received a standard regimen of induction chemotherapy followed by concurrent chemoradiotherapy. Data on demographics, tumor characteristics, treatment response, survival, and toxicities were analyzed.

Results: Of the cohort (n=50), 74% were aged between 41 and 60 years with male pre dominance. Most tumors were moderately differentiated squamous cell carcinomas presenting with proliferative-ulcerative morphology and tumor length

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ranging from 5 to 10 cm. All patients received induction chemotherapy followed by 56–60 Gy radiotherapy with concurrent cisplatin-based chemotherapy. Thirty-two (64%) patients survived beyond two years, and six (12%) achieved a five-year survival. Acute toxicities included Grade II–III esophagitis in 36% of patients, while long-term toxicities such as strictures were observed in 10%. No Grade IV hematologic toxicities were reported. All patients had symptomatic relief in swallowing function during the second week of treatment.

Conclusion: The treatment approach of induction chemotherapy followed by concurrent chemoradiation demonstrated early symptom relief and encouraging long-term survival in medically inoperable patients with middle-third esophageal carcinoma. Careful patient selection and supportive care can mitigate toxicity, making this regime a viable non-surgical alternative.

KEYWORDS

- Carcinoma esophagus • Induction chemotherapy • ChemoRadiotherapy
- Long term survival

INTRODUCTION

Cancer is considered a major health problem across the globe and is the 2nd most common cause of death after cardiac diseases. A significant number of cancers occur in gastrointestinal tract (GIT), of which, colorectal, stomach, esophagus, liver, gall bladder and pancreas are the 6 most common Gastrointestinal (GI) malignancies.^{1,2} Of the total 14,13,316 cancer cases seen in India in 2022 cancer esophagus was 70,637 is 5% of all cancers. (Globocon 2022)

Esophagus is a hollow tubular structure 25 cm in length present in the thoracic cavity and is lined by stratified keratinized squamous epithelium except lower 1/3rd. Histologically, squamous cell carcinoma is most predominant³ followed by adenocarcinoma.^{4,5} Sarcomas and small cell carcinoma account to <1-2% of all esophageal cancers.^{6,7} Moreover, melanoma, leiomyosarcoma, carcinoid & lymphoma is very rare.

Carcinoma esophagus presents with the symptom of dysphagia in 90% patients, odynophagia (50%), weight loss (40-70%).⁸ Risk factors for esophageal carcinoma are cigarette & hookah smoking, red meat, alcohol, tobacco chewing, hot tea consumption, nitrosamines in food, poor oral health, low intake of fresh fruits & vegetables, HPV, obesity, genetic alteration and low socioeconomic status.^{9,10,13} Endoscopic ultrasound and CT Scan are used for proper staging & workup.¹¹ Despite

various advances in the different modalities of treatment, it still carries poor results.¹² A large number of patients succumb to the disease early as most of the patients present in a locally advanced stage and infiltration of disease in adjacent organs and lymph nodes. Trials have demonstrated comparable results for concurrent chemo-radiation versus surgery in locally advanced carcinoma esophagus.¹⁴ The current study retrospectively assesses long-term survival and toxicity profiles in patients treated with induction chemotherapy followed by concurrent chemoradiation in a tertiary care setting.

MATERIALS AND METHODS

It is a Retrospective observational study conducted at a tertiary care center from January 2015 to December 2020. 50 patients with histologically confirmed squamous cell carcinoma of the middle-third esophagus with tumor size of 5–10 cm and medically inoperable due to age, comorbidities, or locally advanced disease were included in the study. The patient should also have completed induction chemotherapy followed by concurrent chemoradiotherapy to a dose of 50.4 to 60 Gy. Induction Chemotherapy with methotrexate 40 mg/M² on day 1 and Cisplatin 30mg /M² day 2 to 5 were given followed by Concurrent Chemotherapy with weekly cisplatin (40 mg/m²) starting on day 21 along with radiation was given. All data was collected from medical records and Demographics, treatment

tolerance, acute and late toxicities (graded as per CTCAE v5.0), and follow-up outcomes were documented. Survival was calculated using the Kaplan-Meier method. Descriptive statistics summarized demographics and toxicity was also noted.

RESULTS

Total 11,468 cancer patients registered in the hospital from 2015 to 2020 and gastrointestinal malignancies were 11.6% of all cancers and cancer esophagus was 44.6% of all gastrointestinal malignancies and 5.2% of all cancers. Of all the cancer esophagus 50 patients who completed the proposed treatment were included in the study. 74% of patients were between age 41 to 60 years with a male predominance. 58% were males and 42% were females. All patients had 5 to 10 cm long growth in middle third esophagus with squamous cell carcinoma histologically. All patients had complaints of dysphagia to solids and semisolids and 17% had absolute dysphagia. Few patients had backache also. 90% of patients had symptomatic relief within the second week and were able to take semisolids and solid diet. 64% patients survived more than two years and 12% for more than 5 years with a median survival of 24.8 months. Only 8% patient had Grade III esophagitis, 40% had grade I - II Nausea and vomiting, 14% Grade II anemia and none had nephrotoxicity or ototoxicity. Esophageal stricture was seen in 10% of patients which required repeated endoscopic dilatation and none of the patients had radiation induced fistula or any other fatal complication.

DISCUSSION

Long-term survival is possible in patients with esophageal carcinoma undergoing induction chemo radiotherapy followed by esophagectomy.¹⁷ out of 44 patients were alive at a median follow-up period of 50 months. 12 of these were disease-free. Only two out of 14 long-term survivors experienced disease-related events after two years, indicating that recurrences are rare after three years.¹⁵

Concurrent chemoradiotherapy (CCRT) is standard treatment for inoperable esophageal cancer, but outcomes remain unsatisfactory. This prompted the investigators to go for consolidation chemotherapy (CCT) followed by

CCRT. A meta-analysis of 11 studies involving 2008 patients showed that while CCT did not improve disease control or objective response rates, it significantly increased the overall survival (OS) and progression-free survival (PFS) without increasing toxicity to lung and esophagus. These findings support the use of CCT after CCRT as a beneficial strategy for improving survival in patients with inoperable esophageal cancer.¹⁶

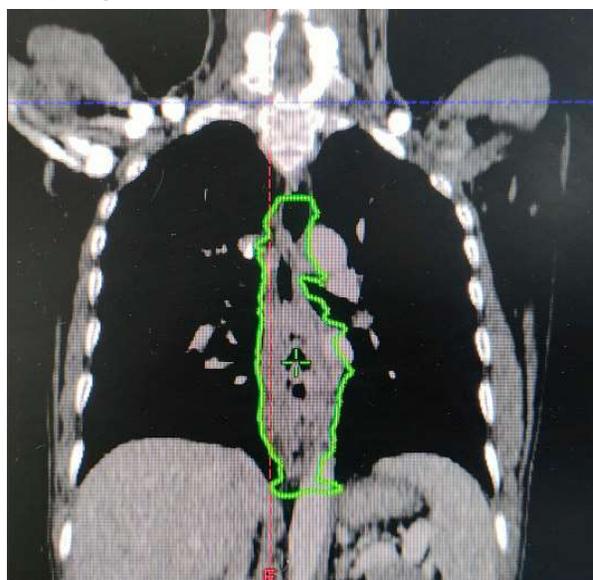


Figure 1: Disease status before concurrent chemoradiotherapy treatment

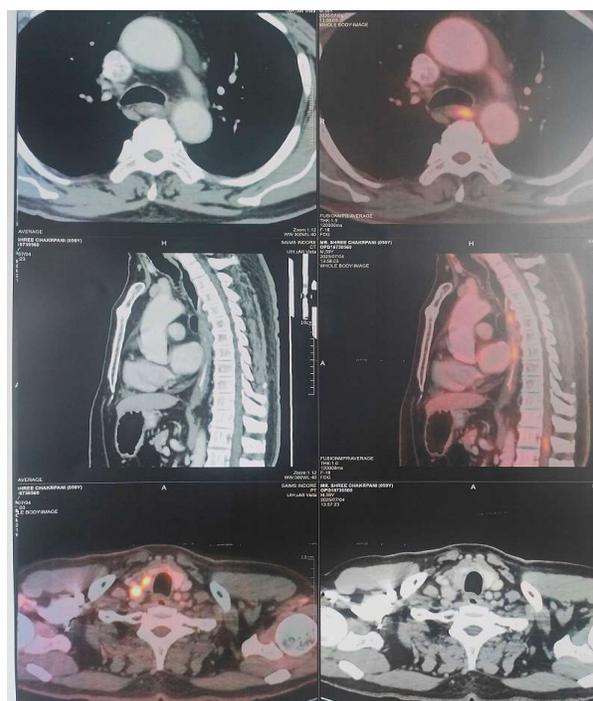


Figure 2: Disease status on PET CT Scan after 6 year of treatment

Induction chemotherapy (IC) followed by chemoradiotherapy (CRT) significantly enhances overall survival (OS) in patients with locally advanced inoperable esophageal squamous cell carcinoma (ESCC), with a median OS of 26.0 months compared to 22.0 months for CRT alone, although it was associated with a higher rate of grade 3–4 leukopenia.¹⁷ In our study also the observed 2-year and 5-year survival rates compare favorably with existing literature, emphasizing the role of aggressive non-surgical therapy in inoperable esophageal carcinoma. The use of induction chemotherapy may help downstage disease and improve the efficacy of subsequent chemoradiation and reducing toxicity with a favorable outcome. The treatment was generally well-tolerated, with manageable acute and late toxicities.

A retrospective study of 122 esophageal cancer patients undergoing an intensive neoadjuvant chemo radiotherapy (nCRT) protocol showed 5-year OS and event-free survival (EFS) rates of 54.8% and 42.7% respectively, with a pathological complete response (pCR) of 71.1% in squamous cell carcinoma (SCC) patients and 37.1% in adenocarcinoma (ADC) patients. ypN+ was identified as a significant negative prognostic factor for OS, while pCR strongly predicted EFS, indicating the nCRT protocol's effectiveness in achieving long-term survival and pCR, warranting further investigation.⁽¹⁸⁾

Gender distribution and histopathological features align with typical epidemiological patterns seen in Indian populations affecting survival. The middle-third esophageal lesions poses both diagnostic and therapeutic challenges due to its anatomical proximity to vital mediastinal structures, making a non-surgical approach not only practical but often necessary.

CONCLUSION

In medically inoperable carcinoma of the middle-third esophagus, the combination of induction chemotherapy followed by concurrent chemoradiation offers a promising balance of efficacy, tolerability and survival. This approach can provide durable control in a subset of patients, as reflected in the five-year survival rate of 12% in this study. Further prospective studies with larger cohorts of patients are warranted.

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