

A Prospective Study on Concurrent Chemoradiation in Inoperable Carcinomas Esophagus

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Abstract

Introduction: Despite many advances in both surgery and radiotherapy, the treatment of esophageal cancer remains a challenge for both surgeons and oncologists. The treatment of choice for patients with carcinoma esophagus is controversial. Recent studies have suggested that combined chemotherapy and radiation therapy may result in improved survival.

Aim: The aim of our study was to analyze the role of concurrent chemoradiation in inoperable carcinomas esophagus.

Materials and Methods: This single-arm prospective study was conducted in the Department of Radiotherapy, Thanjavur Medical College Hospital from August 2018 to August 2019 to analyze the role of concurrent chemoradiation in inoperable carcinomas esophagus. A total of 26 cases of inoperable cases of carcinoma esophagus were treated with once-weekly cisplatin 30 mg/ m² along with radiotherapy 60 Gy in 30 fractions in 6 weeks on telecobalt machine.

Results: Of 26 patients 16 patients were males, 10 patients were females, 17 patients had age <60 years, 9 patients had age above 61 years, 22 patients had squamous cell carcinoma, 4 patients had adenocarcinoma, 4 patients had lesion in upper part of esophagus, 14 patients had lesion in middle part, 8 patients had lesion in lower part, 4 patients had tumor dimension <5 cm, 22 patients had dimension >5.1 cm, 2 patients had tumor stage T1, 22 patients had T2, 2 patients had T3, 1 patient had Nx, 21 patients had No, 4 patients had N1, 15 patients had mild dysphagia, 8 patients had moderate dysphagia, 3 patients had severe dysphagia 1 patients had diarrhea, 1 patient had fatigue, 4 patients had leukopenia, and 1 patient had neutropenia.

Conclusion: Combined modality therapy plays a significant role in the treatment of patients with carcinoma esophagus. Concurrent chemoradiation is a superior treatment in inoperable carcinoma esophagus in terms of local control and survival. Hence, concurrent chemoradiation can also be tried in early cases and surgical morbidity survival and quality of life can be improved.

Key words: Carcinoma esophagus, Cisplatin, Concurrent chemoradiation, Tele cobalt machine

INTRODUCTION

Cancer of the esophagus is a highly lethal malignancy, ranked as the 6th most common cause of cancer deaths worldwide. It is more common in men than women.^[1] High-prevalence areas include Asia, southern and eastern Africa, and northern France.^[2] The median survival is <10 months and <10% of patients survive for 5 years.

Despite many advances in both surgery and radiotherapy, the treatment of esophageal cancer remains a challenge for both surgeons and oncologists. The treatment of choice for patients with carcinoma esophagus is controversial. Management of loco-regional esophageal cancer has undergone a major evolution over the past 25 years. Surgery has long been the standard of care; however, its role has been challenged due to the poor outcome in locally advanced disease. Recent studies have suggested that combined chemotherapy and radiation therapy (RT) may result in improved survival.

Currently, the standard non-surgical treatment of esophageal cancer is concurrent chemotherapy and radiotherapy with results comparable to the best surgical series. The seminal RT Oncology Group (RTOG 85-01)

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www.ijss-sn.com

Month of Submission : 01-2020
Month of Peer Review : 02-2020
Month of Acceptance : 03-2020
Month of Publishing : 03-2020

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trial demonstrated a survival benefit for the addition of cisplatin-based chemotherapy to RT in non-surgically treated patients.^[3,4]

In the RTOG trial 5 years, overall survival in concurrent chemoradiation (cisplatin and 5-fluorouracil [FU] with radiation) group was 26% as compared to 0% in radiation alone group although a higher radiation dose of 64 Gy in 32 fractions was used in radiation alone group as compared to chemoradiation group (50 Gy in 25 fractions).

In the 5 study, in which 5-FU and mitomycin C were used along with radiotherapy 2- and 5-year survivals were 12% and 7% in radiation alone arm and 27% and 9% in chemoradiation arm. Patients treated in the chemoradiation arm had a longer median survival of 14.8 months versus 9.2 months in the radiation alone group.

MATERIALS AND METHODS

A single-arm prospective study of patients undergoes definitive chemoradiation treatment for locally advanced esophageal carcinoma at the Department of Radiotherapy, Thanjavur Medical College Hospital from August 2018 to August 2019 to analyze the role of concurrent chemoradiation in inoperable carcinomas esophagus under different study parameters such as type of carcinoma, site of involvement, stages of tumor involvement, stages of nodal involvement, degree of dysplasia, and tumor dimension. Inclusion criteria include histologically confirmed, potentially unresectable squamous cell carcinoma of the esophagus, Inoperable or locoregionally advanced disease, white blood cells (WBC) count >4000 cells/mL, and platelet count of >100,000 platelets/mL. Exclusion criteria include operable carcinoma esophagus, presence of tracheoesophageal fistula, WBC count <4000 cells/mL, and platelet count of <100,000 platelets/mL.

Staging, including contrast-enhanced computed tomography scan of thorax, abdomen, and upper gastrointestinal endoscopy and biopsy for histological confirmation will be done along with routine blood examinations. All patients will have to sign informed consent forms. Chemotherapy with cisplatin 30 mg/m² alone was given once in a week for a minimum 5–6 times concurrently with radiation. All the patients completed the chemotherapy schedule along with radiotherapy within time and none of the patients required dose reductions due to toxicity. Proper nutrition was maintained during treatment either through Ryle's tube feeding or orally or by intravenous route by parenteral nutrition given during chemotherapy. Patients were admitted only for 1 day every week for chemotherapy. During the treatment, a close observation was kept on the hematological, renal, and nutritional status of the patients

and other toxicities were also noted. Radiotherapy was given on telecobalt machine to the total dose of 40 Gy/20 fractions in 4 weeks to the whole length of the esophagus with anteroposterior portals and then the fields were localized to tumor with 5 cm margins and spinal cord was spared using three fields and a boost dose of 20 Gy/10 fractions in 2 weeks was given totaling to 60 Gy in 30 fractions in 6 weeks. The patients will require to follow-up at 6 weeks from completion of therapy to assess response, toxicity, and disease status. Subsequent follow-up visits will be scheduled at 3 monthly. At follow-up, patients will undergo a thorough clinical examination for the detection of locoregional disease. Patients who drop out or do not complete the planned course of treatment will be excluded and the results were statistically analyzed and discussed.

RESULTS

Of 26 patients, 16 patients were males, 10 patients were females [Table 1].

Of 26 patients, 17 patients had age <60 years, 9 patients had age above 61 years [Table 2].

Of 26 patients, 22 patients had squamous cell carcinoma, 4 patients had adenocarcinoma [Table 3].

Of 26 patients, 4 patients had lesion in upper part of esophagus, 14 patients had lesion in middle part, and 8 patients had lesion in lower part [Table 4].

Of 26 patients, 4 patients had tumor dimension <5 cm, 22 patients had dimension >5.1 cm [Table 5].

Of 26 patients, 2 patients had tumor stage T₁, 22 patients had T₂, and 2 patients had T₃ [Table 6].

Of 26 patients, 1 patients had N_x, 21 patients had N₀, and 4 patients had N₁ [Table 7].

Of 26 patients, 15 patients had mild dysphagia, 8 patients had moderate dysphagia, and 3 patients had severe dysphagia [Table 8].

Of 26 patients, 1 patient had diarrhea, 1 patient had fatigue, 4 patients had leukopenia, and 1 patient had neutropenia [Table 9].

DISCUSSION

Esophageal cancer is usually associated with a poor prognosis due to a high local recurrence rate or distant metastasis.^[6] Although surgery alone or chemoradiotherapy has been widely accepted as the standard treatment

Table 1: Cross-tabulation sex distribution

Sex	No. of patients
Male	16
Female	10

Table 2: Cross-tabulation between age distribution

Age (years)	No. of patients
<60	17
>61	9

Table 3: Cross-tabulation between types of tumor

Type of tumor	No. of patients
Squamous cell carcinoma	22
Adenocarcinoma	4

Table 4: Cross-tabulation between tumor location in esophagus

Tumor location in esophagus	No. of patients
Upper part	4
Middle part	14
Lower part	8

Table 5: Cross-tabulation between tumor dimensions

Tumor dimensions (cm)	No. of patients
<5	4
>5.1	22

for esophageal cancer, the 5-year survival rate is only 20–30%.^[7,8]

It is well known that radiotherapy can cause numerous complications, including radiation esophagitis, radiation pneumonitis, and anorexia.^[9,10] During radiotherapy, dysphagia of patients may become aggravated due to radiation edema of the esophagus, which induces a feeding disturbance. Patients who have undergone esophagostomy also suffer from continual problems associated with the functional domains and specific symptoms.

Anderson *et al.*^[11] used 5-FU and mitomycin C in concurrent chemoradiation group and found a median overall survival of 35 months and a 2 years' survival of 64%. Sischy *et al.*^[12] treated 135 patients with 5-FU and mitomycin C and 40 Gy radiotherapy or radiotherapy alone. The median survival for the multimodality group was significantly longer at 14 months than 9 months for radiotherapy alone.

Table 6: Cross-tabulation between tumor stages

Tumor stages	No. of patients
T1	2
T2	22
T3	2

Table 7: Cross-tabulation between nodal involvement

Nodal involvement	No. of patients
N _x	1
N ₀	21
N ₁	4

Table 8: Cross-tabulation between degree of dysphagia

Degree of dysphagia	No. of patients
Mild	15
Moderate	8
Severe	3

Table 9: Cross-tabulation between toxicity

Toxicity	No. of patients
Diarrhea	1
Fatigue	1
Leucopenia	4
Neutropenia	1

Herskovic *et al.*^[3] randomized 121 potentially curable patients to 64 Gy radiation alone or 50 Gy concurrent with two courses of cisplatin and 5-FU. Long-term follow-up confirms a 3-year survival of 30% versus 0% favoring multimodal therapy.^[4] These trials support concurrent chemotherapy and radiotherapy over radiotherapy alone.

Comparing our study with all others in the literature, we found lower toxicity and almost similar control and mean survival rates. Further, studies with a large number of patients are required to establish that low-dose cisplatin alone used once weekly along with radiotherapy can give similar results with less toxicities and can be well-tolerated by the patients.

CONCLUSION

Combined modality therapy plays a significant role in the treatment of patients with carcinoma esophagus. Concurrent chemotherapy with weekly cisplatin alone gives similar results to cisplatin and 5-FU or 5-FU and mitomycin C as used in other studies with lesser toxicities. Concurrent chemoradiation is a superior treatment in inoperable carcinoma esophagus in terms of local control

and survival. This implies that surgical and non-surgical therapy may be equivalent, especially considering that patients treated with combined modality therapy generally have more advanced disease and are less medically fit than patients who are treated with surgery alone.

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How to cite this article: Vijayakumar S. A Prospective Study on Concurrent Chemoradiation in Inoperable Carcinomas Esophagus. *Int J Sci Stud* 2020;7(12):99-102.

Source of Support: Nil, **Conflicts of Interest:** None declared.