Original Research

Clinical outcomes of definitive chemoradiotherapy for locally advanced unresectable esophageal cancer: An institutional study

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Abstract:

Background: Esophageal cancer presents as a locally advanced disease in majority of the patients. The purpose of this study was to report our experience of the outcomes of definitive chemoradiotherapy in locally advanced unresectable esophageal cancers.

Material & Methods: Patients diagnosed with carcinoma esophagus treated at our center with curative intent with chemoradiotherapy from March 2017 to June 2022 were included in this retrospective study. Pretreatment evaluation and staging was done.The status of the patient was noted at the last follow up. The patients were contacted and their status and survival was updated in June 2023. The statistical analysis was done by SPSS version 25 for demographic details. Control rates and survival were calculated using Kaplan-Meier method.

Results:60 Gy , 50.4 Gy and 35Gy/15# followed by 25Gy /10# were received by 63.6% , 18.2%and 18.2% patients respectively. Only 59.1% patients could receive concomitant chemotherapy with 3 mean no. of cycles. At the median follow up period of 11 months, local control rate is 95.5% , nodal control rate 97.7% , distant control rate was 85 % and overall survival is 91.2%. 52.3% patients had no disease on last follow up.

Conclusion: The study concluded thatradiation is the best modality of treatment in unresectable esophageal cancer patients, especially when combined with chemotherapy.

Keywords: Esophageal cancer, chemotherapy, metastasis.

Introduction:

Definitive chemoradiotherapy is the standard treatment for locally advanced esophageal and unresectable esophageal cancers based on the results of the RTOG-8501 trial.[1] In east Asia, squamous cell histology is more common as compared to western countries where adenocarcinoma of esophagus is predominant.[2,3] A dose ranging from 50.4Gy to 60Gy is usually delivered for such patients, as dose escalation done beyond 60 Gyupto 64.8 Gy, didn't increase the overall survival of patients, as was seen in the INT0123 trial.[4,5] In western countries, the standard accepted radical treatment dose is 50.4Gy whereas in Indian subcontinent, doses upto 60Gy are more commonly used in view of squamous carcinoma histology.[6,7]In accordance with radiobiology of tumors , 45Gy to 50Gy is needed to control microscopic tumors, 60Gy or more is required for gross tumors with conventional fractionation.[8] With advancement of radiotherapy technology, now more conformal methods like 3DCRT, IMRT and VMAT are being used. These methods allow to deliver higher doses to the target with more precision and less toxicity to surrounding normal tissues.[9,10] The purpose of this study was to report our experience of the outcomes of

definitive chemoradiotherapy in locally advanced unresectable esophageal cancers.

Material and methods:

The present study was conducted to assess clinical outcomes in patients diagnosed with locally advanced unresectable esophageal cancer.Patients diagnosed with carcinoma esophagus who were treated at our center with curative intent with chemoradiotherapy from march 2017to June 2022 were included in this retrospective study. There were total 44 patients.Pretreatment evaluation and staging was done withbaseline blood investigations, histopathology,upper GI endoscopy(esophagogastroduodenoscopy) and CECT neck chest abdomen.The patients who had locally advanced or unresectable disease, medically unfit for surgery or refused surgery were treated with chemoradiotherapy. The doses given were 60Gy or 50.4Gy. Eightelderly patients were treated with split course RT with 35Gy in 15 fractions in phase I and 25Gy in 10 fractions in phase II after a gap of two weeks due to their tolerability issues. The response to treatment was evaluated by CECT neck, chest and abdomen after 6 to 8 weeks of treatment according to RECIST guidelines.The status of the patient was noted at the last follow up as having no disease, stable disease, local disease (residual or recurrent), metastatic disease or on palliative treatment. The patients were contacted and their status and survival was updated in June 2023. The statistical analysis was done by SPSSversion 25 for demographic details. Control rates and survival were calculated using Kaplan-Meier method.

Results:

Table 1: Patient Characteristics

Characteristics	Results
Age (years)	
Mean age	**60**
Range	**32-87**
Age groups (years)	**N(%)**
<60	**20(45.5%)**
≥60	**24(54.5%)**
Gender	
Male	**21(47.7%)**
Female	**23(52.3%)**
T Stage	
T2	**10(22.7%)**
T3	**30(68.2%)**
T4	**04(9.1%)**
N Stage	
N0	**28(63.6%)**
N1	**16(36.4%)**
STAGE	
II	**10(22.7%)**
III	**29(65.9%)**
IV A	**05(11.4%)**
SITE	
Cervical	**5(11.4%)**
Upper thoracic	**10(22.7%)**
Mid thoracic	**22(50%)**
Lower thoracic	**07(15.9%)**
Histopathology	
Squamous cell carcinoma	**39(88.6%)**
Adenocarcinoma	**01(2.3%)**
Poorly differentiated carcinoma	**04(9.1%)**

Mean age of patients was 60 years. Maximum patients belongs to age groups ≥60years (54.5%). Maximum patients were female (52.3%). Maximum patients belongs to T3 stage (68.2%) followed by T2 stage (22.7%) and T4 stage (9.1%). Maximum belongs to N0 stage (63.6%) followed by N1 stage (36.4%). Maximum

patients belongs to III stage (65.9%) followed by II stage (22.7%) and IVA stage (11.4%). Most common site was mid thoracic (50%) followed by upper thoracic (22.7%), lower thoracic (15.9%), cervical (11.4%). Histopathology showed that 88.6% patients had Squamous cell carcinoma, 9.1% patients had poorly differentiated carcinoma and 2.3% had adenocarcinoma.63.6% patients received 60Gy radiotherapy dosage, 18.2% received 50.4Gy radiotherapy dosage and 18.2% had split course Radiotherapy. 59.1% patients had concomitant chemotherapy. Mean no. of cycles were 3.The median survival was 11 months. The median local control was 10.5 months. At 11 months ,95.5% of patients had local control, 85% had distant control. At 24 months , the local control was 82% and distant control was 70%.

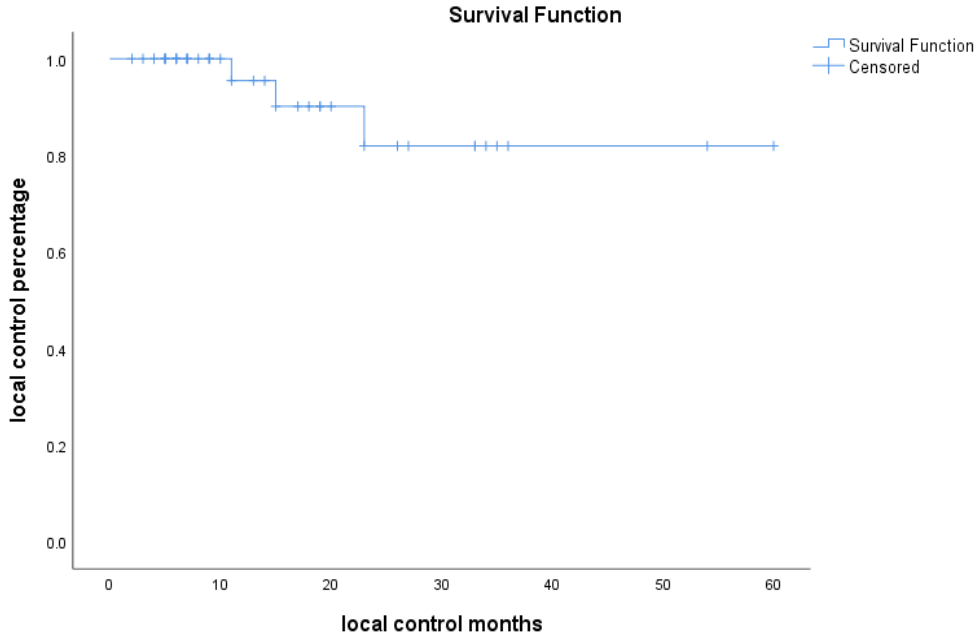
At the end of last follow up of patients, 22.7% patients had residual disease, 4.5% patients had local recurrence, 2.3% patients had nodal recurrence, 15.9% patients had distant metastasis respectively.43.2% patients were on follow up only, 22.7% patients were on Geftinib as they had residual disease, 20.5% patients were on palliative chemotherapy, 13.6% patients were on best supportive care.52.3% patients had no disease on last followup, 11.4% had stable disease, 13.6% who had local disease were on treatment and 13.6% had metastatic disease. 9.1% patients were lost to follow up. At the time of analysis of the study, 08 patients were dead.

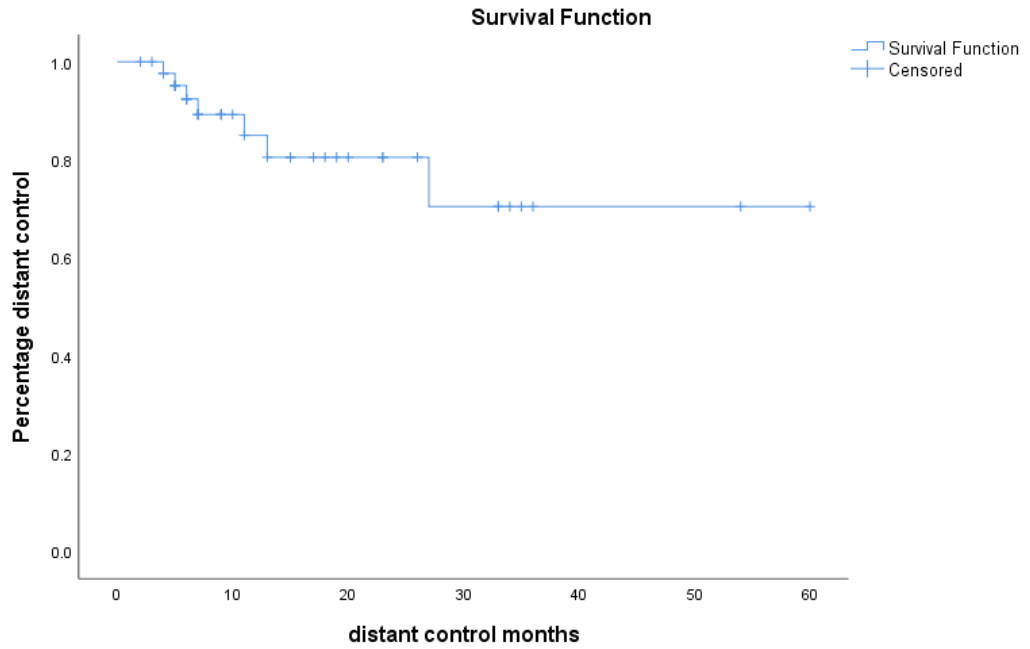
Table 4: Treatment for recurrence

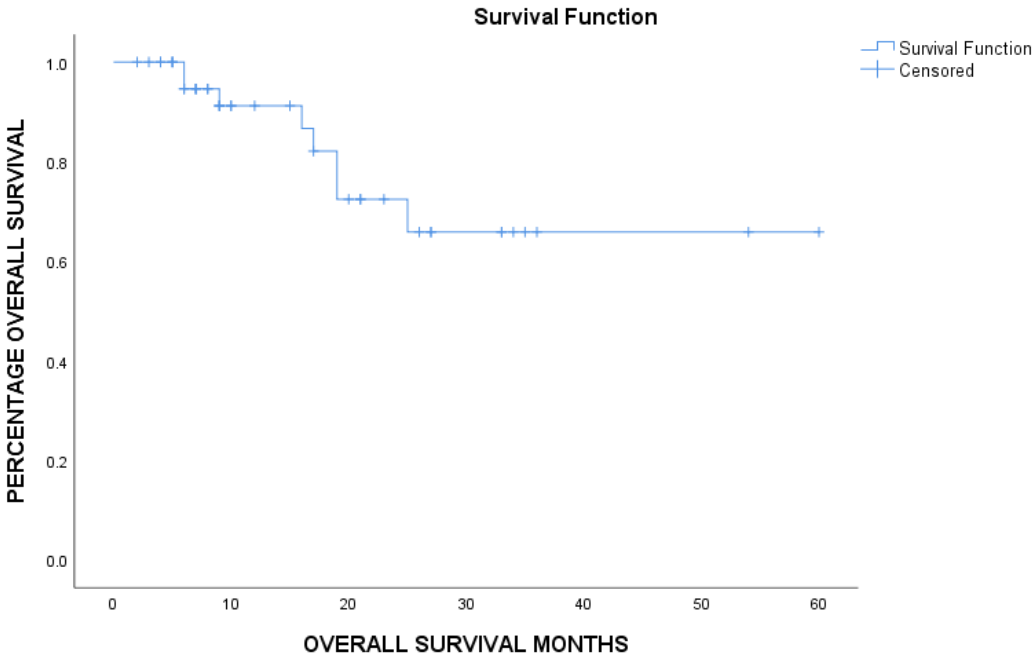
Treatment	(%)
On follow up only	19(43.2%)
Geftinib	10(22.7%)
Palliative Chemo	9(20.5%)
Best supportive care	6(13.6%)

Table 5: Last Follow up

Last Follow up	(%)
No disease	23(52.3%)
Stable disease	5(11.4%)
Local disease on treatment	6(13.6%)
Metastatic disease	6(13.6%)
Lost to Follow up	
Yes	4(9.1%)
No	40(90.9%)







	11 MONTHS	24 MONTHS
LOCAL CONTROL	95.5%	82%
OVERALL SURVIVAL	91.2%	72.4%

Discussion:

Chemoradiotherapy (CRT) plays an important role in the management of esophageal carcinoma (EC) in the neoadjuvant setting for operable patients, and as a definitive treatment for those who are not resectable due to medical or technical considerations.[11,12]In our study mean age of patients was 60 years. Maximum patients belong to age groups ≥60years (54.5%). Maximum patients were female (52.3%). Maximum patients belong to T3 stage (68.2%) followed by T2 stage (22.7%) and T4 stage (9.1%). Maximum belong to N0 stage (63.6%) followed by N1 stage (36.4%).

Maximum patients belong to stage III (65.9%) followed by stage II (22.7%) and IVA (11.4%)respectively. Most common site was mid thoracic (50%) followed by upper thoracic (22.7%), lower thoracic (15.9%), cervical (11.4%) respectively. Histopathology showed that 88.6% patients had Squamous cell carcinoma, 9.1% poorly differentiated carcinoma and 2.3% had adenocarcinoma respectively.In the study by Kapoor et al, the median age of patients was 55 with 67.44% males and 32.56% females. The most common site of tumor was mid thoracic(60.5%) followed by lower thoracic(26.7%).[16] and upper thoracic(12.8%). 64.8% of patients had N0 disease ,15.4% patients with N1, 14.3% with N2 followed by5.5% with N3 disease.[13]S.Ishikura et al in their study had 68 years as the median age of patients. The most common tumour site was mid thoracic(63.4%) followed by upper thoracic(21.1%) which was similar to our study[14]. Noronaha et al in their study had patients of median age of 54 years. Most of the patients had upper third thoracic (34.6%) closelyfollowed by mid thoracic(30.7%) and cervical and lower thoracic were 20.1% and 14.5% respectively. Maximum number of patients had squamous cell carcinoma(92.2%) and belonged to stage III(82.7%) which was similar to our study[15].In our study, 63.6% of our patients received 60Gy, 18.2% received 50.4Gy and 18.2% had split course Radiotherapy. Only 59.1% patients had concomitant chemotherapy and mean no. of cycles were3.At the time of analysis, 22.7% patients had residual disease, 4.5% patients had local recurrence, 2.3% patients had nodal recurrence, 15.9% patients had metastasis. 43.2% patients were on follow up only. 22.7% patients were started on Geftinib, 20.5% patients were planned with palliativechemotherapy, 13.6% patients could receive best supportive care only.52.3% patients had no disease at last follow up, 9.1% patients were lost to followup and at the time of analysis of the study, 08 patients were dead (18.1%)Kapoor R, et aldiscussed the factors affecting compliance to radical treatment of mid thoracic esophageal cancers.Local control and survival rates were much higher in patients who completed treatment as compared to the defaulters. The local control at 1 year was 77.4% and overall survival at 1 year was 75.2%.[13] In our study, patients who had completed radical treatment were included in the study, therefore our local control rates were good (95.5% at median FU of 11 months).[16]Ishikura S, et al evaluated the outcome of 3dCRT with special interest in borderline-resectable disease. Complete response was achieved in 44 patients (42%). At the time of this analysis, 59 patients were dead and 45 were censored. The overall survival for borderline-resectable patients with complete response (CR) and noncomplete response (non-CR) was significantly different ($P < 0.001$), with 3-year survival of 70% and 8%, respectively. With a median follow up of 45 months in unresectable patients with CR and non-CR , the median survival time was 12 and 10 months respectively.[14]Noronha, et al did a retrospective analysis of patients who received weekly paclitaxel 50 mg/m(2) and carboplatin AUC 2 with radical definitive RT for locally advanced esophageal/GEJ cancer. Mean RT dose was 58.7 Gy in 32 fractions over 53 days, with mean of six chemotherapy cycles. Follow-up endoscopy showed remission in 53% and residual disease in 14% which is similar to our study. At a median follow-up of 28 months, median PFS was 11 months (95% CI: 8-13.9), median OS was 19 months Weekly paclitaxel-carboplatin concurrently with definitive RT is efficacious with manageable toxicity.[15]Retrospective analysis done by Suh YG et al et al showed that patients who received ≥50.4Gy dose had significantly better loco regional control (68.7% vs 55.9%).[17] In our study, all patients received ≥ 50.4 Gy . The median overall survival at 11 months and 24 months was 91.2%, and 72.4% respectively. The above data is comparable to our control rates in this study.[17]The drawback of our study was that the patient number of very less, and the median follow upperiod was 11 months only.Also, patients were treated by three different doses of radiation, in accordance to their tolerability, which resulted in unequal patient number distribution between the three radiation dose regimens. Still our study manages to bring out an important fact that chemo radiation is one of the best modality of treatment in the patients who are unfit to go for surgery.

Conclusion:

The study concluded that radiation is the best modality of treatment in unresectable esophageal cancer patients, especially when combined with chemotherapy.More prospective studies with large number of patients and long follow up are needed to predict the survival and local control outcomes of radical chemoradiotherapy.

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