

Patterns of failure in cases of carcinoma of esophagus treated with radical concurrent chemoradiation

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Abstract

Background: Radical chemoradiation has been the main stay of treatment in inoperable cases of carcinoma of thoracic oesophagus. The purpose of the study is to determine the pattern of recurrence after radical concurrent chemoradiation. **Materials and Methods:** Fifty patients with carcinoma esophagus treated with chemoradiation were taken retrospectively for this study. All the patients were treated with external beam radiation therapy (3DCRT/IMRT) of 54 to 59.4Gy with 3 weekly cisplatin 80 mg/m² and capecitabine 1250 mg /m². All patients were followed with upper GI endoscopy at 3-4 monthly for first 3 years, CECT thorax and abdomen at every 3 month for 1 year then 6 monthly up to 3 year thereafter yearly follow up. Appropriate statistics were used for the analysis. All the patient information was taken out from the case files and by telephonic interview. **Results:** 50 patients were included in the retrospective analysis. Median age was 54 years. 26 (52%) were males and 24 (48%) were females. Most common tumour histology being squamous cell carcinoma and most common site being the middle 1/3 of esophagus 30/50(60%). 47/50 (94%) patients received concurrent chemoradiation with cisplatin with capecitabine and 3/50 (6%) received induction chemotherapy with cisplatin and 5-FU. Patients were followed up for a period of 8 months to 34 months (median: 21 months). At the time of last follow up in September 2015, 23/50(46%) patients had local recurrence, 14 (28%) patients had distant failure and 13(26%) patients had no evidence of disease at the time of last follow up. With a median follow up of 21 months, mean overall survival for all the patients was 17.5 months. Patients surviving at the end of 1 year were 68%, at 2 years was 36%, and at 3 years was 4.3%. **Conclusion:** This study concludes that highest incidence of failure and recurrences occur most commonly locally (within the previously irradiated field) even after definitive radical treatment with concurrent chemoradiation. As the local recurrence is more than distant failure we should aim at consolidating the local therapy by dose escalation or alternative radiation therapy.

Key words: Esophageal Cancer, Chemoradiation, pattern of failure

Introduction

Esophageal carcinoma is the eighth most common cancer in the world constituting approximately 6% of all gastrointestinal malignancies and its incidence is raising annually [1]. Surgery is the primary modality of treatment in localized esophageal cancers but the survival rates with only one modality of treatment is very poor with 3-5 year survival rates being only 5 to 20% [2-4]. Multimodality approach with surgery and chemoradiation is the standard of care in present day

scenario. Tumours which are locally advanced are inoperable and are taken up for definitive chemoradiation. This combination of chemotherapy and radiation has an additive effect with respect to increasing the disease free survival rates and also the overall survival of inoperable cases of carcinoma esophagus [4-7]. The dose of radiation for radical intent is similar to the dose used for preoperative chemoradiation i.e. 54-60Gy. Use of more sophisticated treatment modalities such as IMRT have aided in dose escalation to the gross tumour volume and at the same time sparing the normal tissues. Several studies have

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attempted to evaluate the pros and cons of dose-escalations for esophageal cancer. Even after the use of advanced technologies for the treatment, recurrences are common in these patients. This study is done to know the sites of failure in patients with carcinoma esophagus treated with definitive radical intent by concurrent chemoradiation.

Materials and Methods

We retrospectively analysed 50 patients of locally advanced carcinoma esophagus who were treated with concurrent in a regional cancer centre between 2011 and 2014.

All patients were treated with conformal radiotherapy. They underwent a planning computerized tomography (CT) and the GTV was contoured based on the CT scans at the time of evaluation and OGD findings. CTV was contoured by extending the margins to 3cm in superior and inferior direction and 1 cm radially. PTV was generated by adding a 0.5cm margin to CTV. All organs at risk were contoured i.e. heart, lungs and spinal cord. All patients were prescribed to a dose ranging from 54-59.4Gy at 1.8-2 Gy per fraction along with

concurrent weekly cisplatin at 40mg/m² and oral 5-FU in the form of Capecitabine at 1350mg/m² dose. Median overall treatment time for completion of radiation therapy was 48.6 days. Patients were followed up for maximum of 34 months with minimum being 12 months of follow-up.

We assessed the patterns of failure in these patients i.e. local, regional or distant failure based on posttreatment investigations. Barium swallow x-ray and upper gastro-duodenoscopy was performed three monthly for the first one year and thereafter six monthly for the next two years. CT scan of thorax and abdomen with IV contrast was done six monthly for three years. Failure is considered if there is any suspicious lesion which is radiologically documented or pathologically proven.

Any failure within the radiation treatment volume or in the regional lymphatics like mediastinal or supraclavicular or abdominal group is considered to be loco-regional failure and recurrence in any other organ or non-regional lymph nodes is considered as distant failure. All failures are included in the analysis regardless of the timing of failure.

Results

50 patients were included in the retrospective analysis. Median age was 54 years (minimum age 38 years and maximum age 76 years). 26 (52%) were males and 24(48%) were females. Most common tumour histology being squamous cell carcinoma and most common site being the middle 1/3 of esophagus 30/50(60%). 47/50 (94%) patients received concurrent chemoradiation with cisplatin with capecitabine and 3/50 (6%) received induction chemotherapy with cisplatin and 5-FU.

Characteristics	Patients
Sex	
Male	26 (52%)
Female	24 (48%)
Age (yr), Median (range)	54 (38-76)
Primary tumor location	
Upper	10 (20%)
Middle	26 (52%)
Lower	14 (28%)
Histology of primary tumor(SCC)	
G1	18%(36%)
G2	26(52%)
G3	6(12%)
Technique of treatment	
IMRT	8(16%)
3DCRT	42(84%)
Concurrent chemotherapy	
weekly Cisplatin + Cepsitabine	47(94%)
Weekly cisplatin	3(6%)

Patterns of Failure: Patients were followed up for a period of 8 months to 34 months (median: 21months) or till death of the patient. At the time of last follow up in September 2015, 23 (46%) patients had loco-regional failure, 14(28%) patients had distant failure and 13 (26%) patients had no evidence of disease at the time of last follow up.

Loco-regional failure	23(46%)
Distant failure	14(28%)
No evidence of disease	13(26%)

Disease Free Survival: With a median follow up of 21 months, median disease free survival was 14.3 months. Disease free survival at 1 year was 26/50 (52%), at 2 years was 5/13 (38%), at 3 years was 1/23 (4.3%).

Overall Survival: With a median follow up of 21 months, median overall survival for all the patients was 17.5 months. Patients surviving at the end of 1 year were 68%, at 2 years was 36%, and at 3 years was 4.3%.

Discussion

Use of concurrent chemoradiation by radical intent as a standard of care for inoperable cases of carcinoma esophagus has shown poor results [9] in controlling the disease with failure being most commonly occurring at the primary site of the disease. With the advent of advanced technologies for tumour delineation and appropriate treatment delivery, intensification of the local therapy is one of the main aspects of treatment of these tumours [10-12]. Dose escalation at the local site should be considered in treating these patients. This is supported by previous studies demonstrating that for solid tumors, a minimum of 65Gy to 70Gy would be needed for tumour control [13]. While chemotherapy can help to some degree, it does not change the fact that the dose used for radical intent is not adequate to achieve a high probability for local control.

In the previously noted dose escalation trial RTOG 94-05, dose escalation was thought to be ineffective and highly toxic; most of the patients in that study could not receive even a dose of 50.4 Gy owing to toxicity [14]. Thus, dose escalation should be considered keeping in mind several drawbacks associated with it. Given the proximity of the esophagus to the heart and lung, patients should be planned such that dose to these critical structures lies in the acceptable range. High-dose radiation therapy could increase the risk of esophageal stricture and or perforation, a potentially life-threatening complication [15]. It has also been shown that a simultaneous integrated boost IMRT technique could increase the dose to the primary gross tumor by 28% while simultaneously achieving reductions in cardiac and pulmonary doses secondary to improved treatment planning techniques.

In summary, we found that local control after definitive chemoradiation therapy for esophageal cancer remains a problem. It is warranted to explore potential ways of

improving local control including dose escalation, better techniques of treatment delivery such as IMRT. It seems appropriate to evaluate patient-based risk factors such as tumour status, tumour length, and other biological correlates that seem to predict local versus systemic relapses.

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