Quest Journals
Journal of Medical and Dental Science Research
Volume 10~ Issue 3 (2023) pp: 67-70
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

A Prospective Study of Definitive Concurrent chemoradiation in Non operable Squamous cell Carcinoma Oesophagus Patients in a Tertiary care Teaching Hospital in North India(Kashmir)

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Abstract
Introduction: *Despite advances in both surgery and radiotherapy, the treatment of oesophageal cancer remains a challenge for both surgeons and oncologists. The biggest problem affecting patient outcome is late presentation, as most symptomatic patients present with advanced disease. Definitive concurrent Chemoradiotherapy (dCRT) remains as an alternative for those patients unsuitable for surgery due to medical co-morbidities or extensive locoregional disease.*
Objectives: *Aim of this study was to assess the outcome of patients treated with dCRT in our center*
Material and Methods: *The study was done in Department of Radiotherapy and oncology, Government Medical College, Srinagar. It was a single arm prospective study. Sixty consecutive patients with inoperable oesophageal squamous cell carcinoma who met the inclusion criteria were taken for dCRT.*
Results: *Median follow-up was for 19.8 months. Two patients lost to follow-up. The overall survival rate was 83.33% and mean survival period was 19.4 months. Progression free survival was 66.67% with mean progression-free survival duration of 16.5 months.*
Conclusion: *Definitive Concurrent chemo-radiation with was well tolerated, {Paclitaxel50 mg/m^2,injection carboplatin AUC 2(area under curve) }promising a reasonable therapeutic option for patients with inoperable locally advanced squamous cell carcinoma of the oesophagus.*
Keywords: Chemo-radiation, Carcinoma Oesophagus, Overall Survival

Received 06 Mar., 2023; Revised 17 Mar., 2023; Accepted 19 Mar., 2023 © *The author(s) 2023. Published with open access at www.questjournals.org*

I. Introduction

Oesophageal cancer is currently the eighth leading cause of cancer death, comprising 2–3% of all cancer deaths.[1] Single modality therapy with surgery remains the mainstay of curative- intent treatment for early stage cancers. For locally advanced disease, neoadjuvant chemoradiation (chemoRT) followed by esophagectomy is typically standard of care, demonstrating marked benefits in disease control and survival.[2,3,4,5,6,7,8]

In a subset of patients with locally advanced disease who are not candidates for or refuse surgery, definitive concurrent chemotherapy and radiation therapy (DCCRT) is the treatment of choice. To date, there have been several retrospective studies[9,10,11] and few large prospective studies reporting on this approach. One randomized controlled trial compared outcomes in 172 patients with esophageal squamous cell carcinoma (SCC) treated with either induction chemotherapy followed by concurrent chemoradiotherapy (CCRT) and resection, or the same chemotherapy followed by CCRT with an additional 20.0 Gy of RT added instead of surgery. They found no difference in median survival time or 5- and 10- year overall survival (OS) rates, with higher treatment- related mortality observed in patients who received surgery.[12] Similarly, the FFCD 9102 trial

of 444 patients with potentially resectable T3N0- 1M0 esophageal SCC who received induction chemoRT followed by additional chemoRT or surgery found that while surgically treated patients had significantly lower rates of locoregional recurrence (LRR) (34% v 43%) and were less likely to require palliative intervention for dysphagia, they had similar 2- year and median survival as compared to those who continued chemoRT, in addition to having worse quality of life outcomes and increased morbidity acutely. [13]

As DCCRT continues to be used clinically, more data regarding outcomes and toxicities are needed, particularly for the use of more contemporary RT techniques and systemic therapies. This study reports our experience with DCCRT in the treatment of patients with non- operable oesophagus Carcinoma.

Aims and Objective

To assess the outcome of patients treated with dCRT in our center.

II. Material And Methods

Initial assessment: Apart from routine hematological and biochemical lab tests, staging of the disease was done using contrast enhanced computerized tomography (CECT) scan of thorax/abdomen and upper gastro-intestinal endoscopy and biopsy with histological confirmation.

Radiotherapy and Chemotherapy: We used injection Paclitaxel50 mg/m^2,injection carboplatin AUC 2(area under curve) weekly with external radiation for 5 weeks. External radiation dose 50.4Gy in 25 fractions, delivered on Cobalt 60 unit.First 40 Gys were delivered by two anterior portals and boost was given by reduced fields using field technique i.e one another and two posterior oblique fields.

Evaluation of patients during treatment: The regimen was administered on an outpatient basis. During irradiation, all patients were scored weekly during the course of CRT for neutropenia .Clinical examination, complete blood picture, liver and kidney function tests were done before each cycle.

Follow up: The first follow-up was 6-weeks from completion of therapy to assess response, toxicity and disease status. Subsequent follow-up visits were at every three months. At follow-up, patients underwent thorough clinical examination for detection of loco-regional disease. Patients who have not completed the treatment course or lost to follow-up were excluded. Disease progression was considered as clinicoradiological loco-regional disease after complete clinical response to treatment or persistence/increase in disease volume during treatment course

Statistical analysis

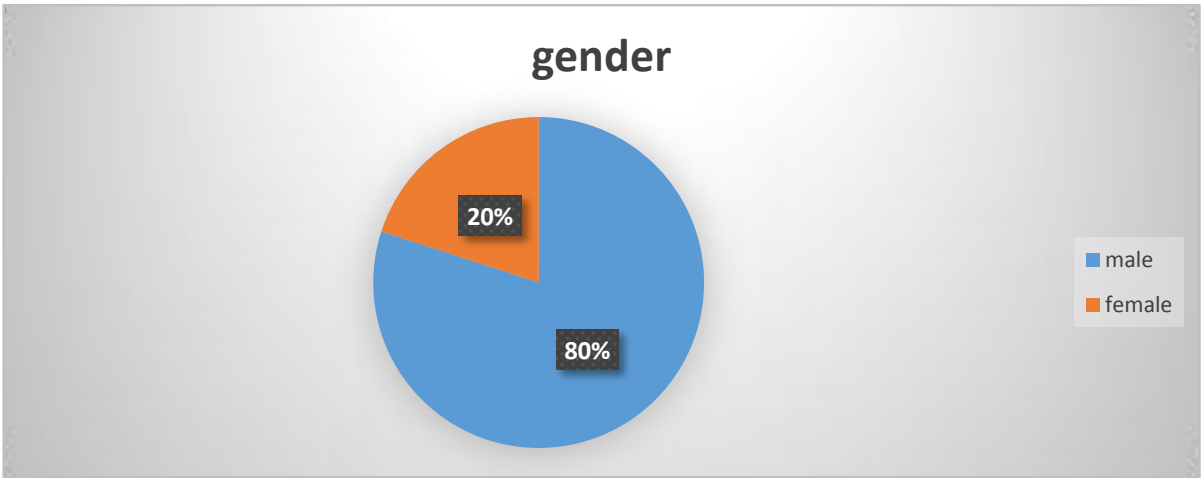
Patient characteristics, responses and toxicities were shown by descriptive methods. Chi-square test was used to compare qualitative variables. The Overall Survival [OS] was defined as the interval between the date of diagnosis and the date of the last follow-up point or death. The OS and Progression Free Survival (PFS) were calculated according to the Kaplan–Meier method. The impact of clinico-pathologic factors (age, sex, site of tumor and stage involvement at presentation) on OS and PFS were examined.

III. Results

Out of the registered 122cases of carcinoma oesophagus during the study period, 62 patients satisfied the inclusion criteria and were taken up for the study after written informed consent.Two patients lost to follow-up.

Gender Distribution

The study group involved 8(20%) females and 32(80%) males.



Age distribution

The median age of the study population was 58.9(45-70) years, majority being between 51 to 60 years.

Table 1: Age distribution

Age	Frequency	Percentage
<50	18	30.0%
51-60	32	53.34%
>60	10	16.67%
Total	60	100.0%

Smoking Habits

Table 2: Smoking Habits

Smoking habits	Frequency	Percentage
Smoker	54	90.0%
Non Smoker	6	10.0%
Total	60	100.0%

Site of Tumour

Ten (16.66%) patients had upper third of the oesophagus as the primary site of the disease, 18(30.0%) had lower third and the majority, 32(53.34%),had middle third as the primary site.

Table 3: Site of tumour

Site of tumour	Frequency	Percentage
Upper third	10	16.66%
Middle third	32	53.34%
Lower third	18	30.00%
Total	60	100.0%

Stage

Fifteen (25.0%) patients had T2 tumor, 36(60.0%) had T3 tumor and 9(15%)had T4 tumor.

Twenty eight (46.66%) patients had N1, 24 (40%) had N2 and 8(13.33%) had N3 nodal involvement.

Stage wise, 40%(n=24) of the patients were stage 3A, 10 %(n=6) were stage2B;stage 3B 20 %(n=12) and stage 3C constituted 30%(n=18) each of the total number of the patients.

Complications

46.66% patients had normal neutrophil count (n=28) and among the remaining patients, grade1 neutropenia was found in eighteen (30%), grade 2 in six (10%), grade 3 in 5 (12.5%) and grade 4 in one (1.66%) patient.

Transient stomatitis was observed in six (10%) patients.

Disease progression

Disease progression and death during treatment or followup was seen in 36.66(n=22) patients whereas the disease not progressed in the rest 38(63.34%).Fifty eight patients completed follow-up and the median follow up duration was 16.8 months.

Survival Rate

The overall survival rate was 83.33% and the mean survival period was 582.7 days (19.4 months). The progression free survival was 66.67% with the mean progression free survival duration of 16.5 months (mean 20.2 months).

The OS and PFS were not significantly related to age and sex of patient or site and clinical stage of the disease.

IV. Discussion

Treatment of carcinoma oesophagus is a nightmare since, at the time of disease presentation, more than a half have metastatic disease, a third have the locally advanced disease and only the rest less than 20% have curable localized disease. The treatment of inoperable oesophageal carcinoma is challenging, and optimal sequencing of treatment modalities remains controversial. While combined modality therapy offers a small but real chance of PFS and potentially prolonged OS, improvement in the quality of life and sustained relief of dysphagia can be achieved in the majority of patients. On this background, we from a Government tertiary care teaching hospital in North India aimed to audit our treatment protocol. So we examined our patients with inoperable oesophageal squamous cell carcinoma undergoing definitive concurrent chemo-radiotherapy (dCRT) for the survival and toxicity profile.

Our study group included 60 patients with a median age of 58.9 years; 80% of them being males. Addiction to smoking, was extremely common (90.0%) in our cohort. Middle and lower third of the oesophagus were the common sites of affection compared to the upper third and the majority presented at 3A, 3B and 3C stage of the disease with only 10% patients in stage 2B.

Median follow-up was for 19.8 months. Two patients lost to follow-up. The overall survival rate was 83.33% and mean survival period was 19.4 months. Progression free survival was 66.67% with mean progression-free survival duration of 16.5 months

Neutropenia was the major toxicity observed. This was comparable to the neutropenia observed in a recent study.[14]46.66% patients had normal neutrophil count (n=28) and among the remaining patients, grade1 neutropenia was found in eighteen (30%), grade 2 in six (10%), grade 3 in 5 (12.5%) and grade4 in one (1.66%) patient.

Two patients died during the treatment whereas the rest completed the treatment without a break. Two patients lost to follow-up.

The overall survival (OS) rate was 83.3% with a mean survival period of 19.4 months. Progression of the disease was noted in 36.66% of patients, and four patients died during the follow-up period. The progression-free survival (PFS) was66.67% with a mean progression-free survival time of 16.5 months.

Results of the present study are comparable to two seminal studies, INT0123trial[15] andRTOG 85-01 trial [16,17] andHowever the toxicities were minimum, compared to as that of RTOG 85-01 trial.

V. Conclusion

Definitive Concurrent chemo-radiation well tolerated, promising a reasonable therapeutic option for patients with inoperable locally advanced esophageal squamous cell carcinoma. One year Overall Survival and Progression Free Survival were comparable with other major trials, showing median survival duration of 19.4 months.

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