

# Palliative treatment with radiotherapy in patients of advanced esophageal carcinoma

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## ABSTRACT


**Background:** Esophageal carcinoma is high prevalence in Asia, including India and most of the patients present in advanced and inoperable stage. Most of the patients have poor nutritional status and low performance status. These patients are unable to tolerate radical treatment. Prognosis of these patients is very poor. There are no enough data of prospective study in palliation of dysphagia of the patients with inoperable esophageal carcinoma with radiotherapy in Eastern India. **Objectives:** The main objective of our study was palliation of dysphagia of the patients with inoperable esophageal carcinoma with radiotherapy. **Materials and Methods:** The study was done with 43 patients with histopathologically proven squamous cell carcinoma and/or adenocarcinoma at thoracic esophagus, intraluminal brachytherapy feasible. Patients were received external beam radiotherapy palliative dose 30 Gy in 10 fractions for 2 weeks followed by intraluminal high-dose rate brachytherapy 6 Gy per fraction per week for 2 weeks. **Results:** In our study, the mean age of the patients was 58 years (age range 48 years–70 years). 1 month after completion of intraluminal brachytherapy, a number of patients with improvement of dysphagia were 34 (79%). The improvement of dysphagia was maintained 25 (73.5%) patients at 3-month completion of treatment and 14 (56%) patients at 6-month completion of treatment. The median duration of dysphagia relief was 5.2 months. Post-radiotherapy complications as chest pain were seen in 10 (23.2%) patients, esophageal strictures were developed in 7 (16.3%) patients, ulcerations were in 4 (9.3%) patients, and esophageal fistula was developed in 1 (2.3%) patient. **Conclusion:** The patients with advanced inoperable or metastatic esophageal carcinoma and poor performance status, palliative radiotherapy are effective modality of treatment for the improvement of dysphagia.

**KEY WORDS:** Inoperable Esophageal Carcinoma; Palliation; Dysphagia; Radiotherapy

## INTRODUCTION

Esophageal cancer is the sixth most common cause of cancer-related deaths worldwide and 3–4 times more common in men than in women.<sup>[1]</sup> It is also high prevalence in Asia,

including India and most of the patients present in advanced and inoperable stage. Most of the patients have poor nutritional and low performance status. Prognosis of these patients is very poor. Most of the patients die due to poor response at primary sites of disease and infiltration of neighboring structures. Tracheoesophageal fistula formation causes aspiration pneumonia leads to death. The primary objective of treatment is palliation of dysphagia. The bypass resection surgery, laser, intubation, chemotherapy, dilatation, external beam radiotherapy, and intraluminal brachytherapy can be done to palliate the dysphagia. The palliation of dysphagia radiotherapy can be administered external beam radiotherapy alone, intraluminal brachytherapy alone, or combination of

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both. Hypofractionated external beam radiotherapy has been applied for palliation of dysphagia with median survival of 5–9.9 months.<sup>[2]</sup> Treatment with intraluminal brachytherapy helps rapid reduction of intraluminal disease and relief painful dysphagia. There are several studies showed that intraluminal brachytherapy alone reduces dysphagia in advanced esophageal carcinoma.<sup>[3-5]</sup> There are no enough data of prospective study regarding treatment with palliative external beam radiotherapy and intraluminal brachytherapy to palliate dysphagia in advanced esophageal cancer in Eastern India. The present study was designed to evaluate disease control at local site, relief from dysphagia, and complications following treatment.

## MATERIALS AND METHODS

The study was done with 43 patients at the Department of Radiotherapy, N.R.S Medical College, Kolkata, between March 2015 and October 2016. Histopathologically proven squamous cell carcinoma and/or adenocarcinoma at thoracic esophagus, intraluminal brachytherapy feasible, ECOG performance<sup>[6]</sup> scale 1–2, and advanced/metastatic disease were included in our study. Pre-treatment evaluation included detailed history taking, through physical examination, upper gastrointestinal (GI) endoscopy and biopsy, CECT scan of thorax, ultrasonography of whole abdomen, CECT scan of whole abdomen as and when indicated, positron emission tomography-computed tomography scan as and when indicated, hematological and biochemical profile, and viral marker were done.

Patients were received palliative external beam radiotherapy with Cobalt 60 Teletherapy machine with dose 30 Gy in 10 fractions for 2 weeks and treatment portals were anterior thorax and posterior thorax fields with dose prescribed to midplane. Intraluminal brachytherapy was done 1–2 weeks after completion of external beam radiotherapy. Brachytherapy was done with MicroSelectron Ir 192 (Iridium) high-dose rate remote control after loading system. Eclipse PLATO treatment planning system was used for brachytherapy planning. The tumor length was determined by upper GI endoscopy, CECT scan before starting radiotherapy. The dose was prescribed 6 Gy per fraction at 1 cm from the central axis of the esophageal catheter. The total dose was prescribed 12 Gy in two fractions at 1-week interval. The treatment length usually includes the entire tumor length at presentation with a margin of 2 cm on either side. After completion of radiotherapy, patients were followed up at 1 month, 3 months, and 6 months to evaluate the primary disease response, relief from dysphagia,<sup>[7]</sup> and post-treatment complications.

## RESULTS

The study was done in 43 patients between March 2015 and October 2016. Patients with advanced/metastatic squamous cell carcinoma and/or adenocarcinoma at thoracic esophagus and intraluminal brachytherapy feasible were included in

our study. All patients received external beam radiotherapy 30 Gy in 10 fractions in 2 weeks followed by intraluminal high-dose rate brachytherapy 6 Gy per week for 2 weeks. The intraluminal brachytherapy was done 1–2 weeks after completion of external beam radiotherapy.

In our study, the mean age of the patients was 58 years (age range 48 years–70 years). Male patients were 33 (76.74%) and female patients were 10 (23.26%). 30 (69.8%) patients had ECOG performance score 1 and 13 (30.2%) patients had ECOG score 2. The most common site of primary disease was middle one-third of esophagus (60.5%) and the most common histopathological type was squamous cell carcinoma [Table 1]. 1 month after completion of intraluminal brachytherapy, a number of patients with improvement of dysphagia were 34 (79%) and 9 (21%) patients showed no improvement of dysphagia. The improvement of dysphagia was maintained 25 (73.5%) patients at 3-month completion of treatment and 14 (56%) patients at 6-month completion of treatment. The median duration of dysphagia relief was 5.2 months. The complete response of disease at primary site was 10 (23.3%), partial response was 25 (58.1%), and non-response and progressive disease were 8 (18.6%) after 1-month completion of treatment [Table 2].

Post-radiotherapy complications as chest pain were seen in 10 (23.2%) patients, esophageal strictures were developed in 7 (16.3%) patients, ulcerations were in 4 (9.3%) patients, and esophageal fistula was developed in 1 (2.3%) patient [Table 3].

**Table 1:** Patients characteristics (n=43)

Characteristics	N(%)
Mean age	58 years (range: 48 years–70 years) (%)
Sex	
Male	33 (76.74)
Female	10 (23.26)
ECOG performance status	
Grade 1	30 (69.8)
Grade 2	13 (30.2)
Histopathology type	
Squamous cell carcinoma	38 (88.4)
Adenocarcinoma	5 (11.6)
Site of lesion in thoracic esophagus	
Upper 1/3 <sup>rd</sup>	6 (13.9)
Middle 1/3 <sup>rd</sup>	26 (60.5)
Lower 1/3 <sup>rd</sup>	11 (25.6)
Dysphagia grade	
Grade 1	23 (53.5)
Grade 2	12 (27.9)
Grade 3	8 (18.6)
Locally advanced and inoperable patients	38 (88.4)
Patients with distant metastasis	5 (11.6)

**Table 2:** Number of patients with improvement of dysphagia after radiotherapy

At follow-up months	Number of patients (%)
1	34 (79) (n=43)
3	25 (73.5) (n=34)
6	14 (56) (n=25)

**Table 3:** Treatment-related complications n=43 (%)

Chest pain	10 (23.2)
Esophageal strictures	7 (16.3)
Ulcerations	4 (9.3)
Fistula	1 (2.3)

## DISCUSSION

Esophageal cancer is the sixth most common cause of cancer-related deaths worldwide and 3–4 times more common in men than in women.<sup>[1]</sup> It is also high prevalence in Asia, including India. In our outpatient's department, most of the patients came in advanced and inoperable stage because the disease is asymptomatic in early stage. Most of the patients have poor nutritional and low performance status. In advanced stage of the disease, curative treatment is limited and palliation of dysphagia is the main objective. In our study, palliative radiotherapy was considered to relief dysphagia due to advanced age of the patients, poor general condition, and locoregional advanced and inoperable/metastasis disease.

In our study, the mean age of the patients was 58 years (age range 48 years–70 years). Male patients were 33 (76.74%) and female patients were 10 (23.26%). 30 (69.8%) patients had ECOG performance score 1 and 13 (30.2%) patients had ECOG score 2. 1 month after completion of intraluminal brachytherapy, a number of patients with improvement of dysphagia were 34 (79%) and 9 (21%) patients showed no improvement of dysphagia. The improvement of dysphagia was maintained 25 (73.5%) patients at 3-month completion of treatment and 14 (56%) patients at 6-month completion of treatment. The complete response of disease at primary site was 10 (23.3%), partial response was 25 (58.1%), and non-response and progressive disease were 8 (18.6%) after 1-month completion of treatment. The median duration of dysphagia relief was 5.2 months. Post-radiotherapy complications as chest pain were seen in 10 (23.2%) patients, esophageal strictures were developed in 7 (16.3%) patients, ulcerations were in 4 (9.3%) patients, and esophageal fistula was developed in 1 (2.3%) patient.

The patients with advanced or inoperable esophageal cancer, good performance status standard treatment is concurrent chemoradiation 50.4 Gy and cisplatin or 5-fluorouracil-based chemotherapy, further dose escalation and minimum morbidity with conformal intraluminal brachytherapy. American Brachytherapy Society recommends for palliative

treatment in esophageal carcinoma with external beam radiotherapy 30 Gy in 10 fractions and intraluminal high-dose rate brachytherapy 10–14 Gy in two fractions.<sup>[8]</sup> Hishikawa *et al.* reported in their study with esophageal carcinoma higher local control rate in external beam radiotherapy plus intraluminal brachytherapy group (62%) compare to external beam radiotherapy alone group (20%).<sup>[9]</sup> Prasad *et al.* reported in their study that median dysphagia score decreased from 4 to 3 in 17 (89.5%) patients of advanced esophageal carcinoma (n = 33) after treatment with external beam radiotherapy and intraluminal brachytherapy.<sup>[10]</sup> Murray *et al.* reported in their retrospective study with locoregional advanced/inoperable or metastatic esophageal carcinoma (n = 148) that improvement of dysphagia was seen in 75% of patients after treatment with palliative external beam radiotherapy to a dose of 20 Gy in five fractions.<sup>[11]</sup> In our study, 1 month after completion of external beam radiotherapy and intraluminal brachytherapy, a number of patients with improvement of dysphagia were 34 (79%) and 9 (21%) patients showed no improvement of dysphagia. The improvement of dysphagia was maintained 25 (73.5%) patients at 3-month completion of treatment and 14 (56%) patients at 6-month completion of treatment. The percentage of improvement in dysphagia in our study (79%) was more compared to Murray *et al.* study (75%) due to addition of intraluminal brachytherapy with external beam radiotherapy. There are many procedures to palliate dysphagia in inoperable esophageal carcinoma and intraluminal brachytherapy is one of the modalities. It can be used alone or in combination with external beam radiotherapy. Intraluminal brachytherapy provides high-dose per fraction to intraluminal tumor resulting in tumor regression and rapid improvement in dysphagia.<sup>[12]</sup>

RTOG 92-07 trial showed that incidence of esophageal fistula was higher 12% in concurrent chemoradiotherapy group, particularly in brachytherapy.<sup>[13,14]</sup> Sharma *et al.* reported in their study that overall complication rates were 30%, with stricture seen in 9 (15%) patients, ulceration in 6 (10%), and trachea-esophageal fistula in 3 (5%) patients.<sup>[15]</sup> Rosenblatt *et al.* reported in their study that the overall complications were perforations 2%, strictures 2%, and fistula 7%.<sup>[16]</sup> Ghosh *et al.* reported that three patients (out of 35) developed ulceration and two developed fistula immediately after treatment and five patients developed stricture.<sup>[17]</sup> Moni *et al.* reported that post-radiotherapy esophageal stricture was the most common complication in esophageal carcinoma and the esophageal stricture was seen in 17–43% of patients.<sup>[18]</sup> Prasad *et al.* reported in their study that 26.3% had persistent chest pain, cough with expectoration in 15.8%, and residual stricture was seen in 57.9%.<sup>[8]</sup> In our study, post-radiotherapy complications as chest pain were seen in 10 (23.2%) patients, esophageal strictures were developed in 7 (16.3%) patients, ulcerations were in 4 (9.3%) patients, and esophageal fistula was developed in 1 (2.3%) patient. In our study, post-radiotherapy complications were almost similar with other studies.

Ghosh *et al.* reported in their study that the median dysphagia-free survival was 6 months.<sup>[17]</sup> Harvey *et al.* reported in their study that the mean duration of dysphagia relief was 4.5 months.<sup>[19]</sup> In our study, the median duration of dysphagia relief was 5.2 months and complete response of disease at primary site was 10 (23.3%) patients, partial response was 25 (58.1%) patients, and non-response and progressive disease were 8 (18.6%) after 1 month completion of treatment.

In our study, patients had inoperable/metastatic stage and poor general condition. All patients received palliative external beam radiotherapy and intraluminal brachytherapy. All patients tolerated treatment well and treatment-related complications were within acceptable limit. However, this study contains a small number of patients and comparatively short period of follow-up that represents a major limitation for the conclusion.

## CONCLUSION

The patients with advanced inoperable or metastatic esophageal carcinoma and poor performance status, palliative radiotherapy are an effective modality of treatment for improvement of dysphagia. High-dose rate intraluminal brachytherapy is safe and most effective rapid relief of dysphagia and tolerated by most of the patients with acceptable toxicity.

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