

## Original Article

# A Combination of Self-Expansile Metallic Stent and External Beam Radiotherapy in Management of Advanced Esophageal Carcinoma with Grade III Dysphagia and Beyond

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ABSTRACT

**Background and Objectives:** Most of the patients of Esophageal Malignancy present in advanced stage. These patients receive palliative treatment. We wanted to evaluate whether combination of SEMS and RT improves the grade of dysphagia. **Methods:** 165 patients diagnosed with Advanced Esophageal Malignancy in middle third of Esophagus with grade III dysphagia were enrolled for the study. Demographic data, grade of dysphagia, improvement in the grade of dysphagia, complications and survival were studied. Follow up was done for a period of 1 year. **Results:** All patients grade of dysphagia improved from grade III- IV to grade I-II. One patient had stent migration. Thirty patients died in one year Followup. **Conclusion:** SEMS along with RT may provide survival benefit in advanced Esophageal Malignancy.

**KEYWORDS:** *Dysphagia, esophageal carcinoma, external beam radiotherapy, palliation, self-expansile metallic stent*

## INTRODUCTION

Esophageal cancer is among the most common causes of death from cancer worldwide.<sup>[1,2]</sup> As the esophagus is distensible, a patient may not recognize any symptom until 50-75 % of luminal diameter is compromised. This explains the association of late clinical presentation with poor prognosis.<sup>[3]</sup> It lacks a serosal lining and has got a rich lymphatic drainage which further increases its propensity to spread to the surrounding structures, thus making it unresectable.

Surgery is the treatment of choice for early esophageal cancers but limited to palliation in patients with advanced disease.<sup>[3,4]</sup> Combinations of self-expansile metallic stent (SEMS) and external beam radiotherapy (EBRT) are newer methods for relief of dysphagia in these patients.<sup>[5-9]</sup>

## Aim of the study

The aim is to study the evaluation of the results of SEMS with EBRT in the management of patients of carcinoma of the middle third of the esophagus and Grade III or more functional grade dysphagia. Functional grades of dysphagia<sup>[5]</sup> are given in Table 1.

## MATERIALS AND METHODS

The study was undertaken for assessing the feasibility and the results with SEMS plus EBRT in patients of carcinoma of the esophagus. Ethical committee clearance was taken for the study. All patients who were taken up in the study were explained about the various modalities of the treatment available. Only those patients who opted willingly were enrolled after taking a valid written consent. One hundred and sixty-five patients were enrolled for the study from patients who reported to surgical gastroenterology clinic for endoscopy in view of dysphagia. All patients had Grade III dysphagia and above, and carcinoma of the middle third of the esophagus as confirmed by endoscopy [Figure 1]. Histopathological diagnosis of the lesions was squamous

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cell cancer. The youngest patient was 35 years old and the eldest patient was 65 years old. There were 35 females and 130 males [Table 2]. All patients were not suitable for surgery at the time of diagnosis as they all were nutritionally poor. Nutritionally poor status was assessed based on the WHO – body mass index <18.5 kg/m<sup>2</sup> (underweight). One hundred and thirty-five patients had disease reaching up to muscularis of the esophagus with mediastinal enlarged nodes on computed tomography (CT) scan.

Any patient not willing to enter study was excluded from the study. Furthermore, patients with lesser grade of dysphagia and esophageal carcinoma not reaching muscular layer were excluded from the study. Cancers of the upper and lower esophagus were excluded from the study. Patients with tracheoesophageal fistula (TEF) were excluded from the study.

After the histopathology report and the CT scan report of patients were available, the patients were admitted

and subjected to dilatation till 9 mm by Savary-Gilliard esophageal dilators (Cook Medical™) under fluoroscopic guidance [Figure 2]. After 24 hours, SEMS named EXPANSE, made by Indus Medical, Kolkata, was deployed across the malignant stricture under fluoroscopic guidance. This stent was made of Nitinol and covered by polyurethane. The patient was admitted and given support of intravenous (IV) fluids until they resumed an oral semi-solid diet. They were then subjected to external beam radiation, 3000 radiations, delivered in 6 weeks (5 days in a week). All patients were assessed every week during the period when EBRT was being given. If needed patients were admitted either for radiation sickness or for EBRT associated dysphagia and in all patients, a check endoscopy was done to see migration of the stent at the end of 2, 6, and 12 weeks in their follow-up period for 1 year. All patients were followed up every month till 1-year poststent deployment. The follow-up visit consisted of general examination, evaluation of dysphagia, and assessment of progress of the disease. Routine laboratory investigations were carried out at the end of every 15 days during the course of EBRT and later every month to see the general condition and nutritional status.

**Table 1: Functional grades of dysphagia**

Grades	Definition
I	Eating normally
II	Require liquids with meals
III	Able to take semi-solids
IV	Able to take liquids only
V	Unable to take liquids but able to swallow saliva
VI	Unable to swallow saliva

**Table 2: Demographic parameters**

Age (years)	Male	Female	Total
35-45	5	1	6
45-55	28	9	37
55-65	97	25	122
Total	130	35	165

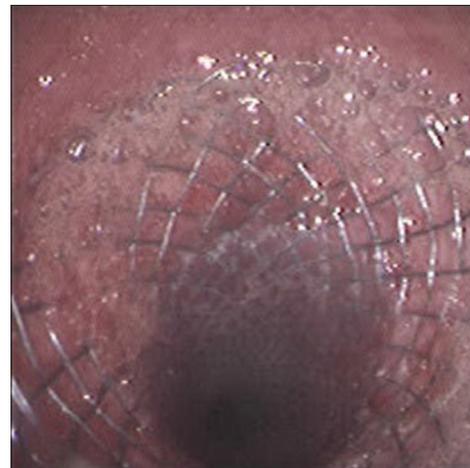
**RESULTS**

All patients had relief of dysphagia within 24 h. Patients could take semi-solid diet within 24 h with minimal or no pain. The dysphagia grade from III to V reduced to dysphagia Grade I [Table 3].

Dysphagia grade before stenting or giving RT was III or more (baseline). Immediately poststenting, the dysphagia improved to Grade I or II in essentially all patients. At the onset of RT, dysphagia seemed to have worsened and grades increased to III or IV. This resolved on



**Figure 1:** Esophageal carcinoma on endoscopy- ulceroproliferative growth



**Figure 2:** “Expanse-” the self-expansile metallic stent placed for esophageal carcinoma (endoscopic view)

completion of the RT sessions. In long-term follow-up, it was observed that there was an improvement in patient symptoms and either there was no dysphagia (Grade I) or patient requires liquids with meals (Grade II). Thus, it was seen that there was 100% relief from the preexisting dysphagia [Table 3].

After stenting, patients general condition improved nutritionally as patient was able to eat food. So these patients were able to tolerate EBRT. Six patients out of 165 had diminished white blood cell counts during some time in their whole course of EBRT [Table 4]. They were treated by admission to ward and administering IV fluids, vitamins, and withholding EBRT for 3 days to a week. Sixteen patients needed admission for blood transfusions as they reported with hemoglobin <8 g/dl. One patient had slippage of stent in 15 days down. He was treated with another stent. Thirty patients died within 1 year [Table 5]. One hundred and thirty-five patients (25 females and 110 males) were alive with near-normal swallowing at the end of 1 year.

Out of 10 female patients who died in 1 year, one female presented with erosion of the innominate artery by the upper end of the stent resulting in massive hematemesis. She died before any endovascular intervention could be done. There was no obvious recurrence of the tumor at the upper end of the stent shown in postmortem report. This patient had reported after 6 months after the placement of SEMS. Four patients (3 males and 1 female) reported with tumor overgrowth and dysphagia within 4 months after the first SEMS placement. In all of them, the second SEMS was placed. Out of 10 female patients who died within 1 year, death in 3 female patients was not related to disease but Cerebrovascular Accident (CVA) in 2 and myocardial infarction in 1. Rest 20 male patients died because of extension of the disease and cancer-related causes. One hundred and thirty-five patients were alive at the end of 1 year without any dysphagia. The patients who survived did not have any slippage of the stent, but the stent seemed incorporated within the wall of the esophagus probably because of radiation-induced inflammation.

## DISCUSSION

Esophageal cancer is now the eight most common type of cancer and the sixth most common cause of death from cancer worldwide.<sup>[1,2]</sup> During the past three decades, many changes have occurred in the epidemiological patterns associated with this disease.

Esophageal cancer has a poor prognosis with overall 5-year survival rate of <10%, and fewer than 50% of patients are suitable for resection at the time of presentation. Esophageal cancer is increasing in last few

**Table 3: Relief of dysphagia**

Relief of dysphagia	Percentage	Special mention
In first 24 h	100% (165/165)	Relief of dysphagia from Grade III, IV, and V to Grade I
At the end of 4 months	97.6% (161/165)	Tumor overgrowth and dysphagia
At the end of 1 year	100% (135/135)	All patients alive

**Table 4: Complications and number of patients affected**

Complications	Percentage of patients affected
Decrease in hemoglobin requiring blood transfusions	96.97% (16/165)
Decrease in WBC counts requiring temporary withholding of EBRT	3.64% (6/165)
Stent slippage	0.6% (1/165)
Erosion of innominate artery	0.6% (1/165)

WBC=White blood cell, EBRT=External beam radiotherapy

**Table 5: Outcome at the end of 1 year**

	Survived (%)	Expired (%)
Total patients - 165	135 (81.8)	30 (18.2)
Male - 130	110 (84.6)	20 (15.4)
Female - 35	25 (71.4)	10 (28.6)

years; unfortunately, the majority of patients will present with locally advanced disease and with local lymph nodal metastasis. As a result, palliation is the best option for this group of patients.<sup>[3,4]</sup>

The aims of palliation are relief of dysphagia and pain, elimination of reflux and regurgitation, prevention of aspiration, and minimizing hospital stay. Without treatment, these patients have a poor quality of life, suffer from rapid weight loss, and experience a relatively quick and unpleasant death from total dysphagia and aspiration of their own saliva.

Current options for palliation include surgical resection, thermal ablation, photodynamic therapy, chemotherapy, chemical injection therapy, argon beam coagulation or bipolar electrocoagulation therapy, enteral feeding (nasogastric, gastrostomy or jejunostomy), and intubation by SEMS, with different rates of success and complications.<sup>[6-8]</sup> SEMS, made up of an alloy usually Nitinol and deployed using fluoroscopy control, is a newer method for relief of dysphagia in these patients.<sup>[9]</sup>

Only RT and only stenting are known ways of palliative treatment for the unresectable patients. However, SEMS with RT has been tried by only few people. Considering this fact that both palliate dysphagia in patients with carcinoma of the esophagus, it is important to offer both

modalities of treatment.<sup>[10]</sup> In this series, we have treated 165 patients who underwent SEMS placement first and RT later.

In a study by Hany Eldeeb and Hend Ahmed El-Hadaad, prospective data of 91 patients with locally advanced or metastatic esophageal cancer who have been treated with either palliative RT, stent, or both were analyzed. Group I had RT only, Group II had stent only, and Group III had both RT and stent. The median overall survival was 169, 119, and 237 in the three groups, respectively. The difference between Group I and III was statistically significant ( $P = 0.01$ ).<sup>[10]</sup> In our series of 165 patients, 110 (81.81%) patients were alive at the end of 1 year and were free of dysphagia.

Majority of the patients suffering from a cancer of the esophagus present with symptoms of dysphagia and weight loss because of an obstructive tumor.<sup>[11]</sup>

Relief of dysphagia occurs rapidly in stent groups than in RT alone group<sup>[9]</sup> and was more so in the stent plus RT group. Recurrence of dysphagia occurred in 8.5% in Group II and 3.8% in Group III. This was due to tumor overgrowth on the stent in Group II. Recurrence of dysphagia was seen in our series in 4 patients out of 165 (2.42%) patients because of tumor overgrowth.

EBRT is known to provide durable and effective relief of dysphagia. However, there is a time lag before symptomatic relief occurs, and up to 6 weeks are required for maximum benefit.<sup>[8]</sup> Survival advantage of combined stenting and RT was first suggested by Ogilvie *et al.*<sup>[12]</sup> Zhong J and Han YT have also investigated the effect of combined stenting and RT on survival of patients of Esophageal Cancer and reported superior results with regard to both relief of dysphagia and survival in these patients. Our 81% of patients were free of dysphagia at the end of 12 months. None of our patients suffered from migration of SEMS post RT.

Slabber *et al.*<sup>[15]</sup> reported 144-day median overall survival, the median radiation dose was  $24.66 \pm 5.07$  in only RT group and  $26.29 \pm 6.17$  in group receiving RT plus stenting, and doses  $>40$  Gy increase toxicity. The median overall survival for stent only patients was 119 days, and these results were similar to that reported by Homs *et al.*<sup>[16]</sup> and Conio *et al.*<sup>[17]</sup>

Han *et al.*<sup>[14]</sup> reported 312-day median overall survival in stent alone patients and 499 days for RT and stent, while Song *et al.*<sup>[18]</sup> reported 161 days, and this advantage may be due to tumor local control by RT.

Yu *et al.* in their trial of offering RT 4-7 days after stent placement reported mean survival of 510 days, but this was a very small series.<sup>[19]</sup>

Rueth *et al.* placed stents in 45 patients for esophageal stricture from esophageal cancer, malignant TEF, and esophageal compression from airway, mediastinal, or metastatic malignancies. Twenty patients had no RT; 25 patients had RT before stent placement, RT after stent placement, or both. Median follow-up was 30 days. Complications requiring stent revision were similar with or without RT. Subjective symptom relief was achieved in 68.9% of all patients, with no differences noted between groups ( $P = 0.99$ ). The 30-day mortality was 15.6%. Patients with RT after stent placement had a longer median survival compared to those without RT (98 vs. 38 days).<sup>[20]</sup> We had excluded the patients with Tracheo-Esophageal fistula were excluded from our study as they were not given RT. Ramakrishnaiah *et al.* in their study of palliation of esophageal carcinoma concluded that among various modalities of palliation such as thermal ablation, chemical ablation, RT, chemotherapy, chemoradiation, palliative surgery and SEMS, SEMS was the best mode of palliation followed by EBRT.<sup>[21]</sup>

## CONCLUSION

Combinations of stent and RT may provide a survival benefit in patients with malignant dysphagia. However, SEMS may have delayed complications such as erosion of innominate artery which is seen in our series. Nearly 81.8% of patients survived for 1-year free of dysphagia suggest reasonable good quality life by SEMS with EBRT in our series.

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## Conflicts of interest

There are no conflicts of interest.

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