# **Original Research Article**

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# Efficacy and risk factor assessment of outcomes of self-expanding metal stents deployed in advanced oesophageal cancer: a case series of 69 patients from a tertiary referral centre of South India

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#### **ABSTRACT**

**Background:** In India, Oesophageal cancer ranks as the 6<sup>th</sup> most common cause of cancer-related deaths. SCC is the most common histology with middle and lower third of the oesophagus as most common location. Often, it is diagnosed in elderly individuals with multiple comorbidities, and at an advanced stage with malignant strictures, where SEMS is treatment of choice. The current retrospective study aims to evaluate efficacy and the risk factor assessment of outcomes of SEMS deployment in patients with advanced oesophageal cancer.

**Methods:** All consecutive patients referred to Department of SGE and LT of BMCRI, with advanced oesophageal cancer from March 2012 to October 2019 were studied. Patients details viz. demography, dysphagia grade, stricture details and SEMS related adverse events and 30-day, 90-day and long-term mortality data was charted and significance of these study parameters along with survival analysis was carried out by using relevant statistical tools.

**Results:** Of the 69 patients, SCC in mid-oesophagus was the most common presentation. 36 patients (52.2%) received prior CRT, TEF (n=11) and distant metastasis (n=7). SEMS intention was palliation in all patients. Overall procedural success using 'Endoscopy alone' was achieved in all 69 patients (100%). Post SEMS period uneventful (n=36), transient haemorrhage (n=5) patients, aspiration (n=11), tumour overgrowth and ingrowth (n=11), SEMS on SEMS (n=5), double SEMS for TEF (n=2). Significant adverse events necessitating reinterventions were seen in 17 patients (24.5%). Kaplan-Meier graph showed lower survival in patients with metastasis and TEF and no statistical difference in-terms of adverse events was noted based on fully covered versus partially covered SEMS.

**Conclusions:** SEMS aids in early resumption of oral feeds and the outcomes of fully covered and partially covered SEMS are comparable in a palliative setting.

# INTRODUCTION

In India, Oesophageal cancer with approximately 47,000 new cases each year, ranks as the 6<sup>th</sup> and 8<sup>th</sup> most common cancer among men and women, and with 42,000 deaths per year, is the 6<sup>th</sup> most common cause of cancerrelated deaths in India. 1,2 Currently, in India, squamous cell carcinoma (SCC) is the most common type of oesophageal cancer, and the most location is the middle and lower third of the oesophagus. 3,4

Oesophageal cancer is asymptomatic in early stages, and often patients seek medical attention only if they have severe luminal narrowing resulting in dysphagia, or present to the hospital with a complication of an advance disease. <sup>5,6</sup> Besides, most of these advanced cancers are diagnosed in elderly individuals who tend to have multiple underlying co-morbidities. <sup>7,8</sup> In such patients, the primary goal is palliation, with an aim to relieve the obstructive symptoms, thereby increasing oral nutrition whilst reducing the risk of aspiration and reflux. <sup>6,9</sup>

Self-expanding metallic stents (SEMS) as a palliative therapy was first described over 20years ago. 10 SEMS is now the treatment of choice for advanced malignant oesophageal stricture.11 In patients with poor functional status and with advanced metastatic disease or in those who cannot tolerate upfront chemo/radiotherapy, SEMS improves the quality of life by relieving dysphagia resulting in optimisation of the nutritional and functional status for subsequent therapy. 11-13 This treatment modality is, however, is not without complications, as published literature suggests a 23-50% incidence of dysphagia following SEMS deployment. 14-16 Factors such location, tumour histology chemoradiation and stent type contribute to recurrent dysphagia.

# **Objectives**

The current retrospective study aimed to evaluate efficacy and the risk factor assessment of outcomes of SEMS deployment in patients with advanced oesophageal cancer.

#### **METHODS**

#### Design and setting

All patients with inoperable carcinoma oesophagus referred to Department of Surgical Gastroenterology and Liver Transplantation (SGE and LT) of Bangalore Medical College and Research Institute (BMCRI) from March 2012 to October 2019 were retrospectively included in this study.

Dysphagia was assessed using the modified Takitas dysphagia grading (grade I: able to eat normally, II: requires liquids with meals, III: able to take only semisolid food, IV: able to take only liquids, V: able to swallow saliva but not liquids, and VI: complete dysphagia).<sup>17</sup>

Stricture details like location, diameter and length were noted.

Adverse events included stent migration, stent obstruction, perforation, haemorrhage and fistula. 30 day and 3 months mortality along with long-term survival were charted.

# **Participants**

All consecutive patients referred to the Department of Surgical Gastroenterology and Liver Transplantation (SGE and LT) of Victoria Hospital and PMSSY Hospital of Bangalore Medical College and Research Institute (BMC and RI), with a biopsy-proven carcinoma oesophagus, or for evaluation of dysphagia and found to be suitable candidates for SEMS placement, were included in the study.

#### Inclusion criteria

Patients with inoperable malignant oesophageal obstruction biopsy-proven with or without tracheoesophageal fistulae, post-operative or anastomotic tumour recurrence or extrinsic compression due to other malignancy.

#### Exclusion criteria

Patients with Stricture within 4 cm of upper oesophageal sphincter, patients with grade 6 dysphasia, uncorrectable bleeding diathesis or those patients in sepsis.

# Pre-SEMS workup

All patients who were referred to Department of SGE and LT of BMC and RI with advance CA oesophagus were evaluated with CECT of thorax and abdomen, upper GI endoscopy with (Fujinon video endoscopy system Gseries and Olympus 150 Series). Paediatric gastroscope was used for stricture of 5-10 mm. Routine blood workup including coagulation profile was a part of the workup.

Modified Takita's grading was used for assessment of dysphasia, this has scores from 1 to 6; grade 1, ability to eat normally and grade 6 with absolute dysphagia.<sup>17</sup>

#### Technique of SEMS deployment

Patient was positioned in left lateral decubitus position in the endoscopy suites and i.v. line was secured with i.v. fluids on flow. SEMS deployment under fluoroscopy was the preferred method in the yesteryears, however in our Department, since the SEMS deployment in the year 2003, it is based solely on endoscopy vision. A paediatric gastroscope was used (if the stricture diameter was <9 mm) to pass the guide wire across the stricture for dilatation. Intravenous tramadol was administered and Savary-Gilliard or wire-guided balloon (CRE) was threaded over the guide wire and the stricture dilation was done up-to 10 Fr. The length of the stricture was measured post dilatation and the interior of the stomach was evaluated as well. The size of the SEMS to be used, would be 2-4 cm longer than the length of the stricture. The available oesophageal partial or fully covered SEMS of 8, 12 and 14 cm with a deployment system, at the time of deployment were used. (Ultraflex®- Boston Scientific; Evolution®- Cook Medical).

We ensured that the opened-out flange after deployment was at least 2 cm above the upper extent of the disease, which constantly would be under endoscopic vision. Post SEMS deployment, the patient was observed in the ward for 24 hours, kept NPO with i.v. fluids on flow. Clear liquids were stared after 24 hours and later progressed to soft diet.

#### Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean±SD (min-max) and results on categorical measurements were presented in number (percentage). Significance was assessed at 5% level of significance.

Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for qualitative data analysis. Fisher exact test used when cell samples were very small. The Kaplan-Meier method was used to estimate the probability of survival past given time points. Survival table, including time, status, cumulative survival and standard error, cumulative events, and number remaining; and mean and median survival time, with standard error and 95% confidence interval. Plots: survival, hazard, log survival, and one minus survival were charted.

# Significant values

+Suggestive significance (p value: 0.05<p<0.10); \*moderately significant (p value: 0.01<p<0.05); \*\*strongly significant (p value: p≤0.01)

# Statistical software

The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data. Microsoft Word and Excel have been used to generate graphs, tables, etc.

#### **RESULTS**

# **Demographics**

Of the total 69 patients, that were included in the study, there were 42 men and 27 women. Overall, the average age of presentation of the cohort was 60.1 years (mean  $\pm$ SD: 60.17 $\pm$ 13.68). The age distribution of men was in the range of 30-90 years with the average age of presentation being 61.1 years. The age distribution for women was in the range of 32-82 years with the average age of 58.8 years. The total study population that was aged above 60 years was 47.8% (Table 1).

Table 1: Age distribution of patients studied.

Age in years	No. of patients	Percentage
<40	3	4.3
40-50	15	21.7
51-60	18	26.1
61-70	20	29.0
71-80	7	10.1
>80	6	8.7
Total	69	100.0

#### Tumour location

The most common location of the tumour based on CT and endoscopy findings was mid oesophagus (n=44, 63.8%) followed by lower oesophagus (n=13, 18.8%) (Table 2).

Table 2: Location of the tumor.

Location	No. of patients (n=69)	Percentage
Upper	8	11.6
MID	44	63.8
Lower	13	18.8
Junction of mid and lower	3	4.34
Junction of upper and mid	1	1.44

#### Disease burden

Among the 69 patients, majority had Takita grade IV dysphagia (n=29, 42.1%) followed by grade III dysphagia (n=25, 36.2%) followed by grade V dysphagia (n=12, 12.3%) (Table 3).

Table 3: Distribution of dysphagia at presentation in our series.

Modified Takita grade <sup>17</sup>	Definition	No. of patients	Percentage
Ι	Eating normally	0	0
II	Liquids with meals	3	4.3
Ш	Semisolids	25	36.2
IV	Liquids alone	29	42.1
V	Saliva alone	12	17.3
VI	Unable to swallow saliva	0	0

Among the patients that were referred to our department, 36 patients (52.2%) received prior chemo-radio therapy, 11 patients (15.9%) had tracheoesophageal fistula (TEF) and 7 patients had metastatic (M1) disease- lung (n=5) and liver (n=2).

In present series, the intention of SEMS deployment in all the patients was for 'palliation'. All the 69 patients needed dilatation (Savary-Gilliard dilatation or CRE balloon dilatation) prior to SEMS deployment. Even though our department has the facility of C-Arm, SEMS was deployed in all the 69 patients using Endoscopic vision alone. Based on availability of appropriate size of covered SEMS at the time of procedure, Partially covered SEMS were used in 29 patients (42.02%) and completely covered SEMS in 40 patients (57.97%).

# Post-SEMS deployment complications

In 36 patients (52.17%) the post SEMS insertion period was completely uneventful. Transient haemorrhage was

noted in 5 patients (7.24%, range 2-4 days), which was self-limiting and did not need any sort of intervention. Post SEMS aspiration was seen in 11 patients (15.94%, range 3-16 days) who had tumour in the lower third of the oesophagus and were all medically managed and dietary advice was reinforced. 14 patients (20.28%, range 25-90 days) tumour overgrowth into the SEMS was noted and of these in 3 patients this was at 18-23 cm and were referred for radiotherapy.

One patient had migration of the SEMS into stomach which was repositioned by pulling on the lasso. One patient, with post CTRT and lung metastasis had perforation following SEMS insertion on day 1. Subsequent contrast study did not reveal any further leak

from the oesophagus. The patient was managed in ICU and unfortunately we lost him on day 28.

In 5 patients a SEMS-on-SEMS had to be deployed for tumour ingrown/overgrowth. In 2 patients both the oesophageal and the tracheal SEMS were used to completely obliterate the TEF.

#### Adverse events

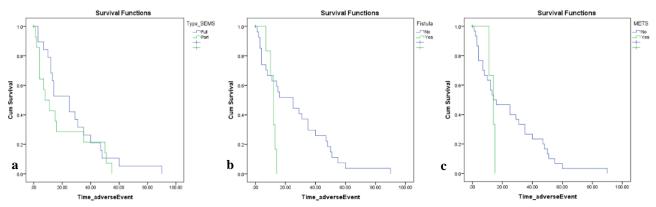
Results of 'time to adverse events' for all the SEMS related complications are as depicted in Table 4. Significant adverse events requiring re-intervention was seen in 17 patients (24.5%).

Table 4: 'Time to adverse events' for all the SEMS related complications.

Event	Number, (percentage)	Average presentation (in days)	Min (in days)	Max (in days)
Aspiration	11, (15.9)	10.5	3	16
Haemorrhage	5, (7.2)	3.4	2	4
Ingrowth	14, (20.2)	44.3	25	90
Pneumonia	1, (1.44)	12	-	-
Perforation	1, (1.44)	1	-	-
Stent migration	1, (1.44)	14	-	-

Table 5: Short and long term survival.

Survival	Number of patients alive (46 out of 69)
30-day	45, (97.8%)
90 day	27, (58.6%)
>90 day	23, (50%)
>6 months	2, (4.3%)



Suggestive of Significance (P value: 0.05<P<0.10). Moderately Significant (P value: 0.01<P<0.05). Strongly Significant (P value: p<0.01).

Figure 1 (a-c): Kaplan-Meier analysis.

The time to death following SEMS insertion was evaluated based on 46 patients (66.6%) as in the other 23 patients, even a telephonic contact was not possible. The shortest duration of survival was 28 days and the longest duration was 15 months (Table 5).

Kaplan Meier function analysis was carried out and the survival function based on presence of metastasis and fistula was estimated, which showed lower survival in those with metastasis (p-value: <0.01) and fistula (p value <0.5). A similar analysis based on fully covered SEMS and partially covered SEMS used did not reveal any significant statistical difference in-terms of SEMS related adverse events (p value >0.5) (Figure 1).

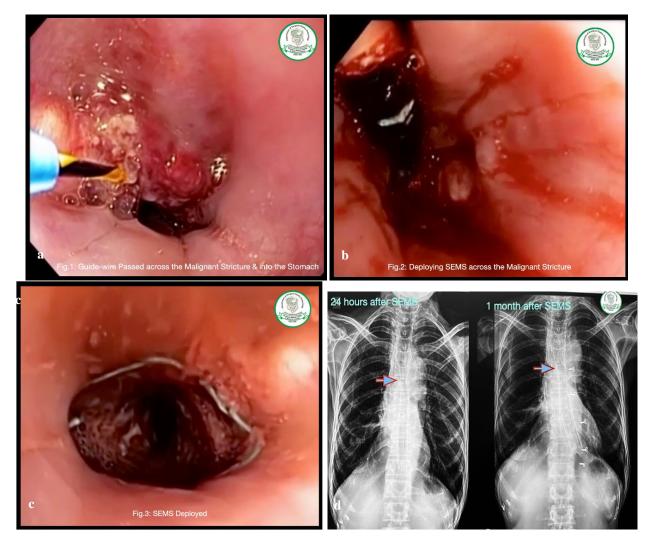


Figure 2 (a-d): Clinical photographs of SEMS; a: Guidewire passed across the malignant stricture, b: Deploying SEMS across the malignant stricture, c: SEMS deployed, d: Chest X-ray after SEMS deployment.

Table 6: Kaplan Meier function analysis for time to adverse event (in days).

Variables	Mean	Median				-		
variables	Estimate	SE	Lower CI	Upper CI	Estimate	SE	Lower CI	Upper CI
Type of SEM	S							
Full	27.26	5.13	17.22	37.31	25.00	6.46	12.35	37.65
Part	18.79	5.33	8.33	29.24	8.00	3.74	0.67	15.33
METS	•		•	•		•		
No	24.70	4.07	16.73	32.67	14.00	7.12	0.04	27.96
Yes	13.33	1.20	10.98	15.69	14.00	2.45	9.20	18.80
Complication	l							
No	26.41	4.40	17.78	35.03	25.00	8.61	8.13	41.87
Yes	11.33	1.02	9.33	13.34	12.00	1.15	9.74	14.26
Overall	23.67	3.74	16.34	30.99	14.00	2.30	9.50	18.50

# **DISCUSSION**

All the cases that were referred to our department were locally advanced oesophageal cancers and squamous cell carcinoma was the most common histology with midoesophagus being the most common tumour location.

Majority of the patients who referred to our department are economically weaker and BPL card holders (below poverty line). Hospital management procures SEMS from Chief Minister Relief Fund, free of cost.

Patients with advanced oesophageal cancer have significant dysphagia contributing to significant weight loss and malnutrition. The options to improve nutrition include nasogastric tubes, SEMS placement, percutaneous endoscopic gastrostomy, surgical feeding gastrostomy/jejunostomy. European Society of Gastrointestinal Endoscopy recommends partial or fully covered SEMS for palliative treatment of malignant dysphagia over laser therapy and oesophageal bypass. <sup>19</sup>

We started deploying SEMS under endoscopic guidance/vision without using fluoroscopy in the year 2003 itself when the affordable Korean SEMS were first made available in Bangalore and we didn't find the necessity of using fluoroscopy at all. Studies show that oesophageal SEMS can be deployed using fluoroscopy or endoscopy and in a palliative setting, the overall outcomes using both the techniques are nearly identical.<sup>20</sup>

In the present study, overall procedural success using Endoscopy alone was achieved in all 69 patients (100%). The advantage of using exclusive endoscopic technique is it is cost effective, avoids unnecessary radiation effects on the patient, the endoscopist and the support staff and can be deployed even in a limited resource clinical setup.

In south of Karnataka, ragi balls is the staple food for most of these patients, which needs to be swallowed without chewing. We strictly advice these patients against swallowing ragi balls or for that matter any food that is not chewed properly. SEMS significantly improves dysphagia and allows for resumption of oral nutrition and it is this resumption of oral feeds and in the context of low survival, leads to an improved quality of life. 21,22

# SEMS for TE fistula

SEMS is the preferred treatment for patients with malignant tracheoesophageal fistula (TEF) and is recommended by ESGE as level III treatment modality, as it offers better quality of life to patients.<sup>23</sup> In the present study, 11 patients presented with TEF and all were managed with oesophageal SEMS and out of these, in 2 patients, tracheal SEMS also had to be deployed to completely obliterate the TEF.

### SEMS and adverse events

In the present study, Post SEMS period was totally uneventful in 36 patients (52.17%), while in 16 patients (23.1%) has adverse events like haemorrhage (n=5)-transient and self-limited and aspiration (n=11)- in patients with tumour in lower third which were medically managed with dietary adjustments. Significant adverse events necessitating reinterventions were seen in 17 patients (24.5%)- tumour overgrowth and ingrowth was noted in 14 patients, out of which 3 patients were referred for radiotherapy. These results are comparable and slightly better than the other published studies. 14,16,24,25

We analysed the contributory role of fully covered SEMS and partially covered SEMS, on SEMS related complications like migration, aspiration and tumour ingrowth, and found no statistically significant difference. These results correlate with the systematic review on this topic.<sup>26</sup>

# Data sharing

All individual-participant data collected during this study will be available, after de-identification, for the purpose of meta-analysis, beginning at 3 months and ending 24 months after publication of this article.

Limitations of this study are it was a retrospective study, possible referral bias as it was a single departmental and single tertiary centre data. Survival details not available in 23 of 69 patients

#### **CONCLUSION**

For advanced oesophageal strictures, covered oesophageal SEMS is an important therapeutic option. With the right technique and patient education, post SEMS period can be without significant adverse events in majority of the cases. We also found in this retrospective study that, in majority of the patients, adverse events with respect to fully and partially covered SEMS were comparable and that the future prospective RCTs focused on this area would help in addressing the clinical and financial aspects.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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