

Self-expanding metallic stent placement with an exaggerated 5-cm proximal tumor covering for palliation of esophageal cancer

Mehdi Tahiri, Pasquale Ferraro, André Duranceau, Melanie Berthiaume, Vicky Thiffault, Moishe Liberman

University of Montreal, Montreal, Quebec, Canada

Abstract

Background The study aimed to evaluate the short- and long-term outcomes with a technique of self-expanding metallic stent insertion in palliative esophageal cancer patients. We hypothesized that a systematic attempt at exaggerated (5 cm) proximal tumor covering could prevent both stent migration and tumor overgrowth/undergrowth.

Methods We reviewed retrospectively all patients who underwent esophageal stenting for palliation of malignant dysphagia over a 24-month period. Consecutive patients were identified from a prospective thoracic surgery interventional endoscopy database. This technique consisted of endoscopic stent insertion with the aim of landing the proximal portion of the stent 5 cm cephalad to the proximal extent of the tumor. All patients were followed at one month post-procedure and every three months thereafter, until death. Short- and long-term complications associated with the procedure and mortality were evaluated.

Results Forty seven patients underwent endoscopic insertion of an esophageal stent in the context of an inoperable esophageal cancer using this technique over a 24-month period. The mean age was 70.4 ± 9.6 years. Four (8.5%) patients underwent re-stenting due to proximal tumor overgrowth. No stent migration, perforation, tumor ingrowth or stent occlusion was reported. The mean patient survival was 146 ± 26.5 days.

Conclusions Esophageal stent insertion under endoscopic guidance with proximal tumor covering of 5 cm is effective and safe. No cases of stent migration and a low incidence of tumor overgrowth/undergrowth were observed with this technique.

Keywords Esophageal stent, self-expanding metallic stent, esophageal cancer, migration, tumor overgrowth, tumor ingrowth

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Introduction

In the United States, 16,640 cases of esophageal cancer were diagnosed in 2010, and there were 14,500 deaths from the disease [1]. The incidence of esophageal cancer is increasing faster than that of any cancer, with a number of cases expected to increase by approximately 140% by

2025 [2]. Unfortunately, more than 50% of esophageal cancers are diagnosed at a late stage, and are inoperable [3]. In this context, a palliative approach is often necessary to alleviate dysphagia.

Multiple randomized trials have demonstrated that self-expandable metal stent (SEMS) insertion is an effective and safe procedure in the palliative treatment of esophageal cancer dysphagia [4,5]. This technique is associated with a few but important complications including perforation, bleeding, stent migration, tumor ingrowth, tumor overgrowth, and stent occlusion [6]. Several studies looking at outcomes from esophageal stent insertion in the literature do not describe the insertion technique [7,8]. In this paper, we describe a novel, modified technique of SEMS insertion in the palliation of esophageal cancer with a 5-cm proximal extension (margin) of the stent above the tumor.

We hypothesized that a systematic attempt at exaggerated 5-cm proximal tumor covering could prevent both stent migration and tumor overgrowth/undergrowth. Our aim was to evaluate the short- and long-term outcomes with a minor

CHUM Endoscopic Tracheobronchial and Oesophageal Center (CETOC), Division of Thoracic Surgery, University of Montreal, Montreal, Quebec, Canada

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Correspondence to: Moishe Liberman, MD, PhD, Associate Professor, Department of Surgery, Division of Thoracic Surgery, Centre Hospitalier de l'Université de Montreal, 1560 Sherbrooke Street East, 8th CD, Pavillon Lachapelle, Suite D-8051, Montreal, Quebec, Canada, H2L 4M1, Tel.: +514 890 8000, Fax: +514 412 7855, e-mail: moishe.liberman@umontreal.ca

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modification to the standard technique of SEMS insertion in the palliation of dysphagia in esophageal cancer patients.

Patients and methods

Study population

Consecutive patients over a 24 months with primary esophageal cancer (adenocarcinoma or squamous cell carcinoma) undergoing SEMS insertion for palliation of malignant dysphagia secondary to endoluminal esophageal tumor were identified from Chum Endoscopic Tracheobronchial and Esophageal Center (CETOC) interventional endoscopy database.

Inclusion criteria were: 1) endoscopic stenting for palliation of dysphagia in esophageal cancer; 2) planned SEMS procedure under endoscopic guidance with 5-cm covering proximal to tumor 3) single stent insertion; and 4) patient deemed unsuitable for treatment with curative intent due to stage, comorbidities or age by a general thoracic surgeon and/or the multidisciplinary esophageal cancer tumor board. Exclusion criteria were: 1) concomitant tracheobronchial pathology (tracheoesophageal fistula, bronchoesophageal fistula, tracheobronchial extrinsic compression by esophageal cancer or malignant lymph nodes); 2) previous SEMS procedure; 3) multiple non-contiguous esophageal tumors; and 4) previous esophageal or gastric surgery.

The study was approved by the institutional review board, Centre de Recherche du Centre Hospitalier de l'Université de Montréal.

Procedure

Patients underwent esophageal stenting under general anesthesia or local anesthesia with sedation. The procedure consisted of esophageal intubation under endoscopic guidance with an adult flexible esophagogastroscope to determine the location, proximal and distal extent, and the length of the tumor. When the tumoral stenosis was too tight to permit passage of the adult endoscope distally, the scope was removed and a pediatric flexible esophagogastroscope was inserted and used to maneuver through the tumor into the stomach.

Once the endoscope was passed distally to the tumor, the scope was passed into the stomach and retroflexed to assess involvement of the cardia. A through-the-scope esophageal guidewire (Hydra Jagwire®, 260 cm length, 0.038 inch diameter, Boston Scientific, Natick, Massachusetts) was inserted into the stomach and the scope was slowly withdrawn with the guidewire in place. Care was taken to record the exact level of the distal and proximal extent of the tumor (distance from incisors) as the scope was withdrawn. The scope was then completely removed with the guidewire remaining in place. An esophageal SEMS was selected with the goals of: 1) providing the patient with the maximal luminal diameter; 2) allowing for proximal covering of the tumor by 5 cm; and 3) complete distal covering

(no tumor visible on endoscopy). The stent was then inserted under proximal endoscopic guidance. Two types of partially covered SEMS were utilized; WallFlex Esophageal Stent® (Boston Scientific, Natick, Massachusetts), and the Evolution Stent® (Cook Medical, Bloomington Indiana). Positioning 5 cm proximal to the tumor was not possible in cases where the proximal extent of the tumor was in proximity to the upper esophageal sphincter. In these cases, the maximal amount of proximal covering possible was utilized. A single stent was used in all cases.

All patients underwent plain film, post-procedure chest x-ray for confirmation of stent position and to allow for a baseline x-ray in order to follow stent migration. Patients were started on a liquid diet within 12 h of the procedure and on a soft diet within 24 h following stent insertion. All patients were followed in the outpatient clinic at one month post-procedure and every three months post procedure until death. Follow-up visits included a chest x-ray and questioning regarding symptomatic dysphagia.

Data collection

Data from each chart was independently extracted by 2 reviewers. Disagreements were resolved by consensus or, when necessary, by a third reviewer. Reviewers extracted information on baseline characteristics of the patients which included gender, age, date of procedure, localization, and length of the tumor. Reviewers extracted data describing the procedure including: type of stent, width of the stent, length of the stent, and the distance from the proximal tip of the stent to the tumor. Short- and long-term complications related to the procedure were evaluated and included: procedure-related death, perforation, bleeding, stent migration, tumor ingrowth, tumor overgrowth, and stent occlusion. Stent migration was assessed based on thoracic surgeon and radiologist reports on routine post stent insertion chest x-rays obtained at one- and three-month intervals until death. All follow up chest x-rays were compared with the baseline chest x-ray obtained immediately following the stent insertion procedure. Survival data were also abstracted from the medical record and in patients where it was not known, referring hospitals and/or families were contacted.

Statistical analysis

Univariate and survival analyses were performed using SPSS Version 17. Survival data were analyzed using the Kaplan-Meier method.

Results

Forty-seven patients underwent insertion of a SEMS in the context of an inoperable esophageal cancer from May 1, 2009 to May 31, 2011. Thirty-eight (81%) patients were male. The mean age of patients at the time of the procedure was 70.4±9.6 years.

The mean tumor length was 8.1 ± 3.0 cm. The median tumor length was 8 cm. Twenty-two patients received concurrent treatment with radiotherapy ($n=9$), chemotherapy ($n=3$), or a combination of both ($n=10$) (Table 1). The location of the tumor was in the upper third of the esophagus in 5 (10.6 %) cases (<24 cm from the incisors), in the middle third in 22 (46.8%) cases (24-32 cm from the incisors), and in the distal third in 20 (42.6%) cases (>32 cm from the incisors) (Fig. 1). All patients had stage III or IV esophageal cancer and were deemed to unsuitable for treatment with curative intent due to stage (assessed by computed tomography, combined positron emission tomography/computed tomography and endoscopic ultrasound), age, or comorbidity by a thoracic surgeon and/or a multidisciplinary esophageal cancer tumor board.

Successful installation of the stent 5 cm proximal to the tumor was possible in 32 patients. In 15 cases, 5-cm proximal covering was not possible due to excessive tumor length or proximity to the upper sphincter. In these 15 patients, 6 patients had their stent placed 3 cm proximal to the tumor, 5 patients had their stent placed 2 cm proximal to the tumor, 1 patient had his stent placed 1 cm proximal to tumor, and 3 patients had their stent placed 0 cm proximal to the tumor.

Table 1 Baseline characteristics of study patients

Characteristics	Median (min-max)
Age (years)	70.1 (40.4-89.3)
Number of male (%)	38 (80.8)
Tumor size (cm)	8.0 (2.0-15)
Tumor localization	
Proximal (%)	5 (10.6)
Middle (%)	22 (46.8)
Distal (%)	20 (42.6)
Distance from the proximal tip of the stent to the proximal extent of the tumor (cm)	5.0 (0-7.0)
Number of patients who received treatment of chemotherapy and/or radiotherapy (%)	22 (46.8)
Number of patients who needed another stent (%)	4 (8.5)

In all cases, the proximal portion of the tumor was completely covered. Fluoroscopy was not utilized in any of the cases, and tumors were never dilated prior to stent insertion.

Among the 47 patients, 37 (78.7%) had self-expanding partially covered metallic esophageal Wallflex® stents (Boston Scientific) inserted, and 10 (21.3%) had Evolution® stents (Cook) inserted. Diameters and length of stents ranged from 20 to 23 mm, and 10 to 15 cm, respectively. Among the 47 stents inserted, 39 (83%) stents inserted in the current study had a luminal diameter of 23 mm, and eight (17%) stents had a luminal diameter of 20 mm.

No perforation, bleeding, stent migration, tumor ingrowth, or stent occlusion was reported. Four patients underwent re-stenting for proximal tumor overgrowth. This occurred at 324, 298, 204, and 160 days following the initial stenting procedure. Among the 4 patients with tumor overgrowth, 2 had their stents placed 5 cm proximal to the tumor, one had his stent placed 3 cm proximal to the tumor, and one had his stent placed 2 cm proximal to the tumor. The tumor overgrowth occurred 324 and 298 days following stent insertion in the patients with the stent 5 cm proximal to the tumor. Tumor overgrowth occurred 204 and 160 days following stent insertion in the patients with the stent placed 2 and 3 cm proximal to the tumor (Table 2). These 4 patients did not receive any concomitant treatment of chemotherapy or radiotherapy.

Tumor overgrowth was treated in all the cases with the placement of an additional stent to cover the tumor overgrowth. In one case, the reason for esophageal endoscopic

Table 2 Complications in the group of patients with a 5-cm proximal tumor covering vs. others

	Group with 5-cm proximal tumor covering ($n=32$)	Group without 5-cm proximal tumor covering ($n=15$)
Number of complications	$n=2$	$n=2$
Type of complications	-Tumor overgrowth 10 months after insertion -Tumor overgrowth 11 months after insertion	-Tumor overgrowth 6 months after insertion -Tumor overgrowth 7 months after insertion

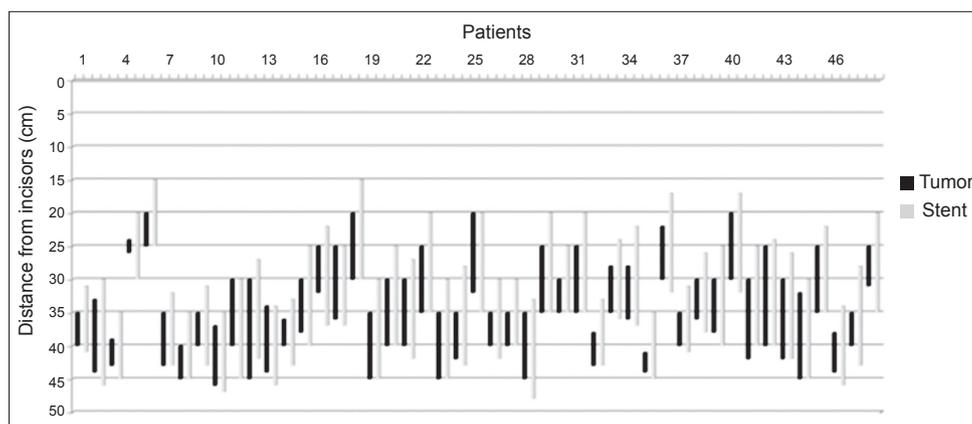


Figure 1 Tumor location and self-expandable metal stent insertion

investigation was tumor bleeding. In this case treatment with endoscopic argon plasma coagulation of the bleeding area of the tumor was employed prior to re-stenting. The mean patient survival following SEMS insertion was 146 ± 26.5 days (Fig. 2). The survival range was between 6 and 636 days.

Discussion

Insertion of SEMS under endoscopic guidance is accepted as a safe and effective method for the palliation of esophageal cancer [9]. The current study evaluated a technique of stent positioning in the treatment of esophageal cancer. The technique consists of a systematic attempt at positioning the stent 5 cm proximal to the tumor under endoscopic guidance, instead of attempting to simply cover the tumor with the stent.

We tried to compare the findings of our study, with studies using similar stents to the ones used in our series, given that radial forces, which may influence the likelihood of perforation or migration, may vary by stent design and manufacturer. We encountered no stent migration in our study, while the reported incidence of stent migration in the literature ranges

from 3% to 18% [10,11]. No patients in the current study had tumor ingrowth, while the reported rate of tumor ingrowth in the literature ranges from 2.5% to 10.5% [12,13]. We did not observe any cases of procedural or peri-procedural perforation, while the reported rate of perforation during stent insertion ranges from 0% to 5% [12-14]. Four patients (8.5%) in the current study experienced tumor overgrowth, comparable with the rate reported in the literature ranging from 2.4 to 25.5% [10,15] (Table 3).

Reasoning behind the 5-cm proximal covering is to allow esophageal mucosal granulation tissue ingrowth into the proximal, non-covered portion of the stent as well as allowing a large portion of proximal normal mucosal apposition to the stent to prevent migration. This mucosal apposition acts as somewhat of a glue to hold the stent in place and prevent migration. The majority of esophageal cancer in the Western world is adenocarcinoma and occurs at or near the gastroesophageal junction and therefore distal overlapping is less important and can actually contribute to stent blocking as the stomach wall can often occlude the distal end of a stent which sits too far in the stomach. Furthermore, based on our and others' experience, these tumors rarely grow significantly distally into the cardia, fundus and body over time and therefore distal overlapping is less necessary [16-18]. No cases of tumor undergrowth (tumor growing distal to the stent) were observed in the current study.

Eighty three percent of stents inserted in the current study had luminal diameters of 23 mm, the largest diameter that exists in commercially available SEMS. By oversizing the luminal diameter of the stents, even in very severe stenoses, we believe this technique provides a better palliation of dysphagia, but also decreases migration due to the radial force of the stent pushing on the tumor and the esophagus. Our preference is to always use a 23 mm diameter stent and to reserve smaller diameter stents only for cases of extreme stenosis or for cases of tumors pushing the trachea or left mainstem bronchus for fear of causing airway obstruction. We were able to insert these large diameter stents at no expense to perforation. There were no perforations in the current cohort. We do not dilate tumors and allow the SEMS to gradually dilate the tumor over the first 48 h.

SEMS complications can be costly, both for the healthcare system due to the need sometimes for a second procedure and

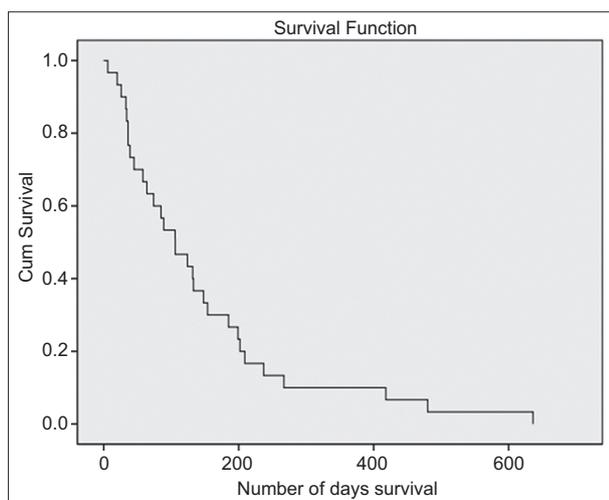


Figure 2 Kaplan-Meier survival curve

Table 3 Complication rates reported in the literature

Study characteristics			Complication rates					
Authors	Year	Sample size	Perforation rate	Stent migration rate (%)	Tumor ingrowth rate (%)	Tumor overgrowth rate (%)	Re-stenting (%)	Mean survival
Current study	2014	47	0	0	0	8.4	8.4	146
Dobrucali <i>et al</i> [8]	2010	90	0	4.4	3.3	6.6	15.5	134
Wilkes <i>et al</i> [10]	2007	98	0	3.1	-	25.5	39.8	100
Sarper <i>et al</i> [12]	2003	41	4.9	2.4	2.4	2.4	-	94
Wengrower <i>et al</i> [15]	1998	81	3.6	5.95	0	2.4	-	120
Adam <i>et al</i> [14]	1997	42	0	19	9.5	2.3	36	53
Kozarek <i>et al</i> [11]	1996	38	3	18.4	5.2	23.6	-	90

potential hospital admission, and for the patient [19]. Previous studies have tried to find solutions to address stent migration associated with SEMS [20,21]. Endoscopists have used clips to stabilize the stent, in an attempt to prevent stent migration. Kato *et al* described 9 patients who underwent stent insertion with clip stabilization, 3 for stricture and 6 for fistulas. None of the patients experienced stent migration, however 3 patients experienced delayed complications (perforation and obstruction) related to stent insertion. Vanbiervliet *et al* reported on 23 patients who underwent stent insertion with clips for esophageal strictures and fistulas. In this study, 3 patients (13%) experienced stent migration. We believe the technique described in the current study is simpler and more reliable than clipping due to the fact that it does not add any additional intervention or time to the stent insertion procedure. Also, it does not add to the risk of the procedure (no additional foreign body or risk of mucosal tear). Furthermore, the described technique aims to prevent not only stent migration, but also tumor overgrowth and occlusion related to stent placement. The mean survival in the current cohort following stenting was 146 days. The mean survival following stenting varies widely in the literature from 53 to 198 days, comparable to the mean survival in the current study [13,14].

To our knowledge, this is the first study that describes and evaluates this technique of stent insertion in malignant esophageal tumors. The technique is associated with fewer short- and long-term complications compared to the insertion techniques reported in the literature.

Limitations of the current study include the retrospective nature of the data collection and the lack of dysphagia scoring pre- and post-procedure in the patient cohort. However, the aim of the study was to evaluate the success and complication rates associated with this modification to the insertion technique. Furthermore, several studies have demonstrated that dysphagia is significantly relieved in most patients undergoing SEMS insertion [22-24]. Another limitation of the study is the absence of comparison with a control group of patients treated with a SEMS without proximal tumor covering of 5 cm. Finally, in our study 83% of stents used had a luminal diameter of 23 mm, the largest diameter that exists in commercially available SEMS. We would like to acknowledge that our low migration rate could be a combination factor of our 5-cm exaggerated covering of the proximal tumor and the wide length of the stents used.

In conclusion, the technique we describe in this paper is safe, accurate and possibly associated with fewer complications than traditional techniques reported in the literature. Further research is needed to assess with more accuracy the benefits of exaggerated 5-cm proximal tumor covering with SEMS. Endoscopists using SEMS in the palliation of dysphagia should consider this adaptation to the traditional technique of SEMS insertion for the palliative treatment of esophageal cancer.

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Summary Box

What is already known:

- Self-expandable metal stent (SEMS) insertion is an effective and safe procedure in the palliative treatment of esophageal cancer dysphagia
- SEMS insertion is associated with few but serious complications including perforation, bleeding, stent migration, tumor ingrowth, tumor overgrowth, and stent occlusion
- The majority of studies evaluating outcomes following esophageal stent insertion in the literature do not describe their insertion

What the new findings are:

- Stent placement with an exaggerated 5-cm proximal covering of the tumor is safe, reproducible, and possibly associated with fewer complications than traditional techniques reported in the literature

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