Research Article

Self-expandable metallic stents for the palliation of malignant dysphagia: a single center experience

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Abstract

Introduction: Self-expandable metallic stents (SEMS) for the palliation of unresectable esophageal cancer (EC) is now standard of care. We evaluated the technical success, clinical outcomes, and safety of endoscopic SEMS placement in patients with unresectable EC.

Methods: Retrospective cohort analysis of endoscopy data on all patients with unresectable EC referred for stent placement. Dysphagia scores, pre and post SEMS placement, were calculated in order to define clinical success of SEMS treatment.

Results: A total of 42 patients (28 male, mean age = 73.1 years) underwent endoscopic SEMS placement: 38 (90.5%) with primary esophageal tumor and 4 (9.5%) with an extra-esophageal mass. Tumors were located in the distal n=33 (78.5%), mid n=7 (16.7%), and proximal n=2 (4.8%) esophagus. Technical success of stent placement was 41/42 (97.6%). One technical failure required a second stent placement. Clinical success was achieved in all patients (100%) with significant improvement in dysphagia score. The mean pre-SEMS dysphagia score was 2.88 and the post-SEMS dysphagia score was 1.04 ($p<0.00001$). A total of 13 (30.9%) patients required re-stenting within a mean of 32 weeks due to tumor ingrowth/overgrowth (n=8), stent migration (n=4), or stent degradation (n=1). No immediate adverse events (AE) occurred. Early AE (within 1 week of stent placement) occurred in 6 (14.3%) patients: vomiting (n=3), stent migration (n=2) and chest pain (n=1). Late AE occurred in n=11 patients: death (n=6) unrelated to stent placement, globus sensation /recurrent dysphagia / food impaction (n=5), and stent migration (n=1). Median survival was 17 weeks.

Conclusions: Endoscopic placement of SEMS for palliation of dysphagia due to unresectable EC is technically feasible, effective, and safe.

Key words: Dysphagia, Esophageal Cancer, Palliation, Stent

INTRODUCTION

The incidence of esophageal cancer continues to increase in the United States, and is currently the fastest rising incident cancer [1]. In the United States alone, an estimated 17,990 new cases of esophageal cancer were expected to be diagnosed in 2013, with 15,210 esophageal cancer-related deaths [2]. Worldwide an estimated 482,300 new esophageal cancer cases were diagnosed and 406,800 cancer related deaths occurred in 2008 [3]. The American Cancer Society estimates that 16,980 new cases of esophageal cancer (men 13,570, women 3,410) will be diagnosed in the United States in 2015 and 15,590 persons (men 12,600, women 2,990) are expected to die of the disease [1].

Unfortunately, the majority of cases of esophageal cancer are diagnosed at an advanced stage [4]. Therefore, most esophageal cancers are unresectable at the time of diagnosis and thus palliative therapy is the only treatment option [5]. The goals of palliative therapy are to improve dysphagia, maintain oral intake and nutritional requirements, relieve pain/discomfort, and improve health-related quality of life [6, 7].

The popularity of self-expanding metal stents (SEMS) as a means for palliation in esophageal cancer has been steadily rising over the past decade [8]. In their 2013 guideline on the role of endoscopy in the assessment and treatment of esophageal cancer, the American Society for Gastrointestinal Endoscopy recommended esophageal stenting as the preferred method for palliation of dysphagia in patients with esophageal cancer [9].

The aim of this study was to analyze and report on our institutional data regarding the procedural success and clinical efficacy of endoscopic stent placement in patients with unresectable esophageal cancer. We also report the incidence of early and late adverse events, need for repeat stenting, and patient survival.

METHODS

This was a retrospective cohort study whereby we reviewed the endoscopic database of the Institute of Gastroenterology at the Rambam Healthcare Campus, Haifa, Israel. Using endoscopy codes, we identified all patients who were referred for malignant related esophageal stricture between January 1, 2009 and December 31, 2013, and who underwent endoscopic placement of an esophageal stent(s) for palliation of dysphagia. Three interventional endoscopists (IK, KY, AS) placed all of the esophageal stents reported in this study.

All endoscopic procedures were performed with the patient under moderate sedation (endoscopist-administered balanced propofol sedation using midazolam, fentanyl and propofol and using a standard gastroscope (GIF-1T160; Olympus, Tokyo, Japan) and fluoroscopy [10].

Post SEMS placement, all the patients were recommended to take high dose PPI to prevent GERD symptoms.

The esophageal tumor was demonstrated through video endoscopy with tumor size, location, and malignant histology documented in the endoscopy report. If necessary, bougie (Savary-Gilliard) dilation was performed immediately prior to stent placement to allow passage of the endoscope. The esophageal stent was then placed using a guide-wire, and deployed under direct endoscopic and/or fluoroscopic view. A stent at least 2 to 4 cm longer than the malignant stricture was used, which allowed the stent to extend at least 1 to 2 cm above and below the proximal and distal margins of the tumor. Technical success of stent placement was defined as adequate deployment and positioning of the stent at the site of the malignant stricture. The type of stent selected was according to the availability of esophageal stents that were in stock in our endoscopy unit at the time of the endoscopic procedure.

Data Collection

All endoscopy reports were reviewed and data regarding patient age, gender, tumor size, tumor location (upper/middle/distal esophagus), histopathology, stent type, and stent size were recorded. Data regarding any previous therapies including: chemotherapy, brachytherapy, and/or surgical treatment were also collected. Dysphagia scores, pre and post esophageal stent placement, were calculated using the Dysphagia grading system [11]. The post stent placement dysphagia score was evaluated within 24-48 hours following stent placement. This grading system consists of five discreet dysphagia grades: Grade 0 = able to eat a normal diet; Grade 1 = able to eat some solid food; Grade 2 = able to eat semi-solid diet only; Grade 3 = able to swallow liquids only; Grade 4 = unable to swallow liquids (complete dysphagia). The clinical efficacy of the esophageal stent was *a priori* defined as an improvement of at least 1 dysphagia grade following stent insertion [12].

The safety of SEMS placement was evaluated by evaluating the incidence of serious adverse events. Adverse events were evaluated and divided according to period of time: Immediate adverse event: during the procedure and included technical difficulties in stent insertion/placement, major bleeding, aspiration, perforation, life threatening adverse event, and death. Early adverse event: occurring within one week of stent placement and included major bleeding, chest pain, perforation, stent migration, globus sensation, aspiration pneumonia, or other. Late adverse event: from eight days and up to one month following stent placement and included globus sensation, chest pain, stent migration, major bleeding, perforation, tracheo-esophageal fistula formation, tracheal compression, recurrent dysphagia due to tumor ingrowth/overgrowth or food impaction, gastroesophageal reflux, aspiration pneumonia, or other.

Patient follow-up was carried out up to two years following initial esophageal stent placement and the need for repeat stenting for any reason was documented and reported upon. Prior to initiating our data collection, we received local Institutional Review Board (Rambam Health Care Campus Helsinki Committee) approval to review our endoscopic database and report upon these de-identified patient data.

Table 1. Baseline characteristics of patients

Characterstics	No.
No. of patients	42
Sex(M/F)	28/14
Mean age, years(range)	73(34-91)
Location of obstruction	
Proximal-esophagus	2
Mid-esophagus	7
Distal-esophagus	33
Histology	
Squamous cell carcinoma	9
Adenocarcinoma	29
Extrinsic	4
Dysphagia score before stent placement	
2	5
3	34
4	3

RESULTS

Patients

Between January 1, 2009 and December 31, 2013, a total of 42 patients (28 males (66.6%), mean age 73.1 years (age range 34-91 years)) underwent palliative endoscopic esophageal stent placement for unresectable esophageal stricture of malignant origin. Baseline patient characteristics are presented in Table 1.

Indication for Esophageal Stent Placement

All patients had unresectable, advanced stage malignancies. Thirty eight were intrinsic

Table 2: Characteristics of patients before and after the intervention

Case	Gender	Age	indication	stage	location	stent type	DS before	DS after
1	Male	68	AC	4	Lower	Evolution	2	1
2	Female	62	AC	3A	Lower	Hanaro	3	1
3	Female	83	AC	4	Lower	Evolution	3	1
4	Female	79	SCC	3	Lower	Evolution	3	1
5	Male	66	SCC	4	Upper	Evolution	2	0
6	Male	80	AC	4	Lower	Evolution	2	1
7	Male	68	AC	3	Middle	Evolution	2	1
8	Female	34	SCC	4	Lower	Evolution	3	0
9	Male	61	AC	4	Lower	Evolution	3	2
10	Male	77	SCC	4	Lower	Ultraflex	3	1
11	Male	83	AC	4	Lower	Evolution	3	0
12	Female	86	AC	4	Lower	Ultraflex	2	1
13	Male	58	SCC	3A	Lower	Ella	3	2
14	Male	57	NSCLC	4	Middle	Ultraflex	3	2
15	Male	66	AC	4	Lower	Evolution	3	1
16	Male	81	AC	4	Lower	Ultraflex	3	1
17	Male	86	SCC	4	Middle	Ultraflex	3	1
18	Female	94	SCC	3B	Middle	Ultraflex	3	1
19	Male	58	NSCLC	4	Middle	Ultraflex	3	1
20	Male	61	SCC	4	Upper	Ultraflex	3	1
21	Male	85	AC	4	Lower	Evolution	3	1
22	Male	83	AC	3B	Lower	Ultraflex	3	1
23	Female	61	AC	4	Lower	Evolution	3	2
24	Female	80	AC	4	Lower	Ella	3	1
25	Female	54	AC	4	Lower	Evolution	3	1
26	Male	83	AC	4	Lower	Ultraflex	4	1
27	Male	74	AC	4	Lower	Evolution	3	1
28	Male	85	AC	4	Lower	Evolution	3	2
29	Female	65	AC	4	Lower	Evolution	3	2
30	Male	82	AC	4	Lower	Hanaro	3	1
31	Male	91	SCC	4	Lower	Evolution	3	2
32	Female	91	AC	3B	Lower	Ultraflex	3	1
33	Female	69	BC	4	Middle	Evolution	3	2
34	Male	91	AC	4	Lower	Evolution	3	1
35	Male	89	AC	3B	Lower	Evolution	3	1
36	Male	88	AC	4	Lower	Evolution	4	1
37	Female	77	AC	4	Lower	Evolution	3	1
38	Male	56	AC	3C	Lower	Evolution	3	0
39	Male	48	AC	4	Lower	Evolution	3	0
40	Female	85	AC	4	Lower	Evolution	3	1
41	Male	68	NSCLC	3A-B	Middle	Evolution	4	1
42	Male	59	AC	4	Lower	Ultraflex	3	0

AC- Adenocarcinoma, SCC- Squamous cell Carcinoma, NSCLC- Non Small cell lung Cancer, BC- Breast cancer, DS- Dysphagia score

esophageal malignancies (adenocarcinoma (n=29) and squamous cell carcinoma (n=9)). The remainder (n=4) had an extrinsic mass compressing the esophagus resulting in dysphagia (3 non-small cell lung cancers and 1 metastatic breast cancer). The majority of esophageal tumors were located in the lower third of the esophagus / gastro-esophageal junction, n=33 (78.5%); n=7 (16.7%) were located in the middle third of the esophagus, and n=2 (4.8%) were located in the proximal esophagus (table 2).

Esophageal Stent Type

A total of 43 stents were initially placed endoscopically. Two biodegradable Ella stents (ELLA-CS, Czech Republic) and 41 esophageal self-expandable metal stents: Partially-covered Evolution stent (Cook Medical, Bloomington, Indiana, USA, n=27), partially-covered Ultraflex stent (Boston Scientific, Marlborough, MA, USA, n=12), fully-covered Hanaro stent (M.I. Tech, Seoul, Korea, n=2) and (See Table 2).

Clinical Outcomes and Adverse Events

Technical success was achieved in 41/42 (97.6%) patients. One technical failure required a second stent to be placed. This single technical failure occurred during an attempt at placing an Ultraflex stent in the proximal esophagus in a patient with squamous cell carcinoma. This necessitated the placement of a second SEMS (Evolution stent) during that same procedure. A total of 37/42 (88.1%) of the cohort had a pre-SEMS dysphagia score of 3 (able to swallow liquids only). The clinical success of SEMS placement was achieved in all 42/42 (100%) patients, with all patients having improvement of at least one grade in their dysphagia score The mean pre-SEMS dysphagia score was 2.88 and the post-SEMS dysphagia score was 1.04 ($p<0.00001$).

Early adverse events were reported in 6 patients, including vomiting (n=3), recurrent dysphagia due to stent migration (n=2), and chest pain (n=1). Late adverse events were reported in 11 patients, including death thought unrelated to stent placement (n=6), recurrent dysphagia (n=4), two of those were due to food impaction and two due to stent migration (most likely due to reduction in tumor size), and globus sensation (n=1) in which inflammation around the Ella stent was observed at repeat gastroscopy. The migrated stents included Hanaro (n=2), Ella (n=1) and Ultraflex (n=1). The stent migration rate for SEMS was 1/39 (2.5%).

Table 3. Characteristics of patients with repeat stent insertion

Characterstics	No.
Total	13
Type of first stent	
Evolution	6
Wallflex	5
Other (Hanaro/Ella)	2
Cause of obstruction	
Stent migration	4
Overgrowth/ingrowth	8
Food impaction/other	1
Type of second stent	
Evolution	4
Wallflex	4
Other (Hanaro/Ella)	5
Location of obstruction	
Proximal-esophagus	0
Mid-esophagus	4
Distal-esophagus	8

Repeat Esophageal Stenting

A total of 13 / 42 (30.9%) required a second stent placement: Evolution stent (n=4), Ultraflex stent (n=4), Hanaro stent (n=2), and biodegradable Ella stent (n=3). All patients needing repeat stenting had recurrent dysphagia caused by stent migration (n=4), tumor ingrowth/overgrowth (n=8), or complete degradation of the Ella stent (n=1) (Table 3).

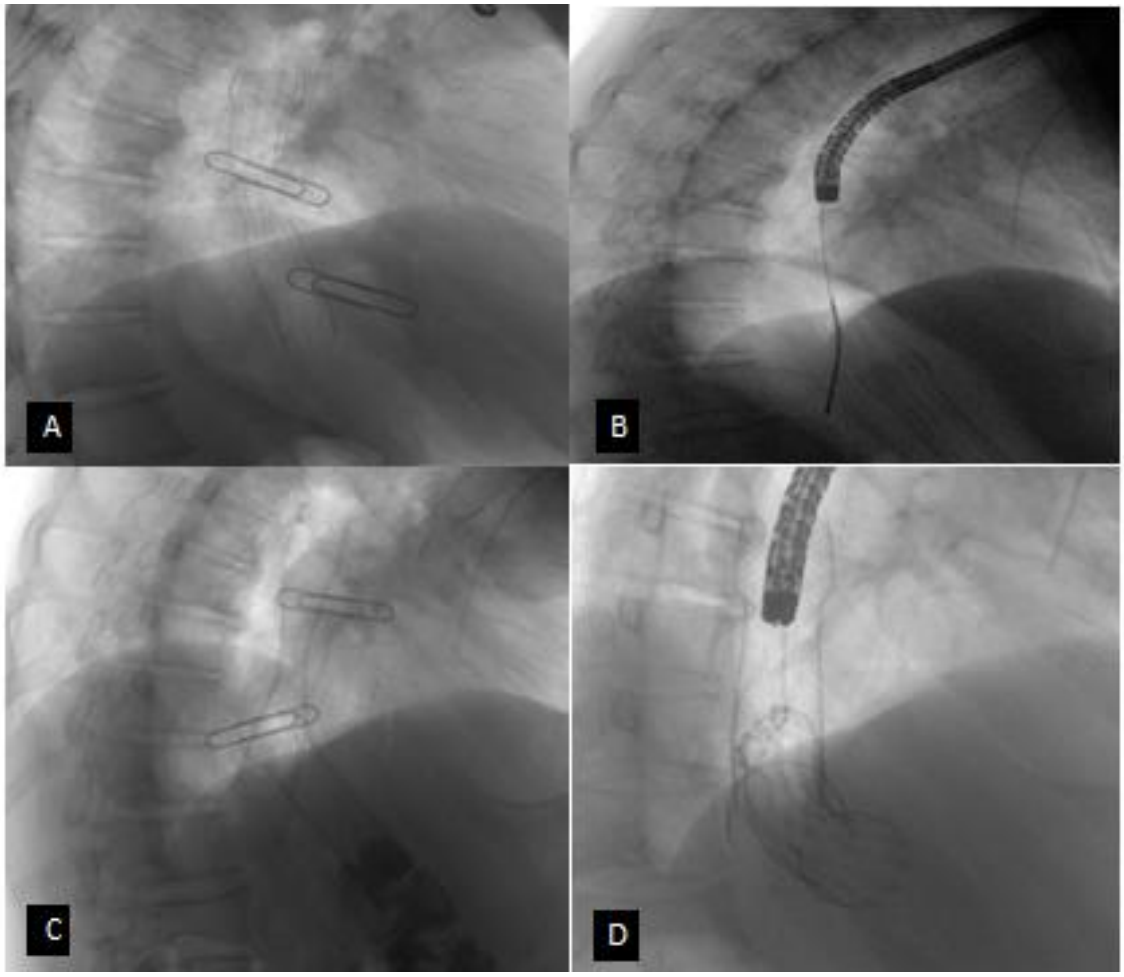

Figure: A patient with migrated stent, second stent insertion and retrieval of the first stent (see text).A, first stent insertion. B, Migrated stent in stomach, Savary-Gilliard dilatation before second stent insertion. C, Second stent in place, migrated stent in stomach. D, Endoscopic retrieval of the migrated stent through the second stent.

Regarding the location of esophageal obstruction and need for repeat stenting, 57% (4/7) of the mid-esophagus obstruction cases required repeat stent insertion duo to recurrent dysphagia, in comparison to 24% (8/33) of the distal esophageal obstructions. This difference was statistically significant ($p<0.05$).

The mean time to second SEMS placement was 32 weeks following initial stenting. One patient with a gastroesophageal junction adenocarcinoma had recurrent dysphagia 9 weeks after stent insertion (Ultraflex stent, Boston Scientific, Marlborough, MA). The stent migrated to the stomach. A second stent (Evolution stent, Cook Medical, Bloomington, Indiana, USA) was inserted (after a Savary-Gilliard dilatation). One week later, the migrated stent was endoscopically retrieved through the second stent (figure). Adverse events within 30 days associated with second stent placement occurred in six patients including death (n=2, unrelated to stent placement), recurrent dysphagia caused by tumor ingrowth/overgrowth (n=3), and one patient complained of persistent dry cough (n=1). Median

survival of this cohort from time of initial esophageal stent placement was 17 weeks.

DISCUSSION

Esophageal cancer was the sixth most common cause of cancer death in 2008, which led to 406,000 deaths worldwide with more than 80% of the esophageal cancer cases occurring in developing countries [1,15]. The prognosis of esophageal cancer is poor since most esophageal tumors are diagnosed at a late stage, with a five-year survival rate less than 20% due to the presence of locally advanced disease and undetected metastatic disease at the time of diagnosis [16]. Dysphagia is the predominant symptom in more than 70% of patients with advanced esophageal cancer [17]. Many types of palliative therapies, or combination of therapies, have emerged in recent years such as endoscopic metallic stents, external beam radiation, brachytherapy, chemotherapy, chemo-radiotherapy, laser treatment and photodynamic therapy. Despite recent progress in therapeutic methods, the optimal intervention has not been established. Endoscopically placed esophageal stents are increasingly being used to palliate dysphagia, because they offer a quick, safe and fairly easy treatment option. The main advantage of stenting over other treatments is a noticeable relief of dysphagia immediately after the procedure [13, 14].

In this single-center study, we evaluated outcomes of esophageal stents in patients who underwent palliative endoscopic esophageal stent placement for unresectable esophageal disease. We found that technical success in stent placement was very high (41/42, 97.6%) and also clinical success (improved dysphagia score) was achieved in all patients (100%). There were no immediate serious adverse events or mortality during stent placement. The most common adverse event encountered was recurrent dysphagia due to stent migration or tumor overgrowth, both usually requiring repeat stent placement. Re-stenting procedures also demonstrated excellent technical and clinical success, and offered an easy and effective solution to recurrent dysphagia. These results compare favorably with other studies, and add to the published literature showing effectiveness of this endoscopic treatment.

The primary rationale in using covered SEMS is to prevent tumor ingrowth, however, this is balanced by higher rates of stent migration. Uncovered SEMSs, while they rarely migrate, have a relatively high restenosis rate due to tumor ingrowth/overgrowth over time. Partially-covered SEMSs, on the other hand, have the advantage of both low migration and low restenosis rates [18, 19]. We primarily placed (39/43, 91%) partially covered SEMSs of two types: Evolution stents (27/39, 69%) and Ultraflex stents (12/39, 31%). However, this study is too small to be able to compare adverse events and efficacy with other stent types. A total of 13/42 (30.9%) patients required a second stent due to stent obstruction/migration with recurrent dysphagia. The stents that were replaced were: Evolution n=6, Ultraflex n=5 and other stent type n= 2 (Table 3).

In this study, all but two of the malignant esophageal obstructions were located in the middle or distal third of the esophagus. Proximal esophageal obstructions are considered to be a relative contraindication for stent insertion due to the potential for technical difficulties and the risk for laryngeal compression. In such cases, maximal caution should be used while inserting the stent. Proximal release stents or through-the-scope stents can minimize the risk.

In summary, the palliative treatment of patients with inoperable esophageal cancer using self-expanding metal stents appears to be a safe and effective therapy. In our experience, esophageal stents offer an effective treatment option for

palliation of dysphagia in patients with malignant disease. Overall relief of dysphagia was achieved with minimal adverse events and with no need for secondary re-intervention in the majority of patients. Importantly however, in those cases of recurrent dysphagia, repeat endoscopic stent placement is an effective intervention.

Abbreviations

AC, Adenocarcinoma
AE, adverse event
BC, Breast cancer
DS, Dysphagia score
EC, esophageal cancer
GERD, gastrointestinal reflux disease
NSCLC, Non Small cell lung Cancer
SCC, Squamous cell Carcinoma
SEMS, self-expandable metal stent

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