Acceptable results after self-expanding metallic stent treatment for dysphagia in non-resectable oesophageal cancer

Ole Steen Bjerring, Torsten Pless, Claus Fristrup & Michael Bau Mortensen

ABSTRACT

INTRODUCTION: Dysphagia is the most common symptom of malignant obstruction in the oesophagus and at the gastro-oesophageal junction (GEJ) region, and the relief of dysphagia plays a major role in palliative treatment of this condition. The aim of the present study was to evaluate the need for and nature of re-intervention after self-expanding metallic stents (SEMS) insertion in patients who were palliated for cancer of the oesophagus or GEJ.

MATERIAL AND METHODS: At a third-level referral centre in Denmark, all SEMS procedures were prospectively registered for SEMS characteristics and procedural events and data regarding re-interventions and survival were retrieved retrospectively in a six-year inclusion period.

RESULTS: A total of 108 stents were inserted into 87 patients (63 males and 23 females) with a median age of 71 years (range: 41-94 years). The primary SEMS used was Ultraflex in 77, Cook or Choo in seven and Wallstent in three cases. All but one SEMS were successfully placed, and no perforations occurred. Fifty patients had their dysphagia scores recorded. The average score before and after stent insertion was 2.4 and 0.8, respectively, ($p < 0.01$). Two-thirds of the patients needed late re-interventions. The most common problem was tissue/tumour ingrowth (n = 40). Seven patients (8%) experienced stent migration. The average re-intervention rate was 2.8 per patient. The median survival after SEMS was 116 days (range 2-866 days). The median time to first re-intervention was 44 days.

CONCLUSIONS: SEMS treatment was a safe and effective palliation of malignant obstruction in the oesophagus and GEJ region, but the procedure was associated with a frequent need for re-interventions.

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Dysphagia is the most common symptom of malignant obstruction in the oesophagus and at the gastroesophageal junction (GEJ) region. Since a minimum of two thirds of the patients are beyond curative surgical treatment, either because of advanced disease or concurrent disease [1], dysphagia relief plays a major role in their palliative treatment [2]. Several principles have been introduced in order to achieve an acceptable ability to swallow. Three methods seem to prevail: local thermal ablation (Argon beaming), endoscopic placement of self-expanding metallic stents (SEMS), or brachytherapy. According to international literature, the latter two have been the most widely used in recent years [3]. These two principles have been found to be equal with regard to dysphagia-related quality of life [4], but due to the immediate effect of SEMS compared with the later onset effect of radiation and the relative short life expectancy for these patients, SEMS is often the treatment of choice. However, SEMS is not without problems, and a number of re-interventions are needed, although data on how many and why have seldomly been published [5, 6].

The aim of the present study was to evaluate the need for and nature of re-interventions after SEMS insertion in patients with cancer of the oesophagus or GEJ.

MATERIAL AND METHODS

Since January, 1998 all patients treated with SEMS at the Department of Surgery, Odense University Hospital, have been prospectively registered in a database with regards to SEMS type and procedural complication. Data regarding re-intervention and long-term complications were retrospectively assessed from the patients' medical records and cross-checked with the regional patient administrative system (FPAS) in a study period lasting from January 1998 to December 2003. All patients living in the county of Funen and treated with SEMS for malignant disease in this period were included. Information about the time of death was retrieved from the Danish Central Person Registry (CPR-registret).

SEMS placement was indicated when the tumour was found to be either clearly stenotic or non-passable with a standard endoscope over a distance of minimum 2 cm and covering more than three-quarters of the circumference. Dysphagia was classified as:

0 = able to eat normal diet/no dysphagia, 1 = able to swallow some solid foods, 2 = able to swallow only semi-solid foods, 3 = able to swallow liquids only, and 4 = unable to swallow anything/total dysphagia [7].

Patients with a dysphagia score of 0 or 1 would not be considered for primary SEMS or re-intervention. The patients received sedo-analgesia (benzodiazepine/opi-

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Surgical Department A, Odense University Hospital

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ate combination), and the procedures were performed with diagnostic or paediatric endoscopes combined with X-ray visualization. Covered SEMS were used as standard. The cover length was calculated as the length of the tumour plus 10-15 mm. The standard choice of SEMS type was the Ultraflex (Boston Scientific) in lengths of 10-15 cm, a cover of 7-12 cm, a body diameter of 18 mm and a flange diameter of 23 mm. Fully covered SEMS was used in patients with airway fistulas. In case of short luminal recurrence after primary treatment, the shortest available lengths of the Choo or Z-stent (Solco Intermed and Wilson-Cook) were preferred.

When deployed, expansion and positioning of the stent were evaluated with both X-ray and endoscopy in order to assure sufficient stent position and tumour coverage. Advancement of the endoscope through the newly placed SEMS was not attempted.

After discharge, all patients were given access to a hotline and instructed to make contact in case of renewed dysphagia. If the dysphagia was scored 2 or above, a new endoscopy would be scheduled within a couple of days. If tissue overgrowth was encountered during the re-interventional procedure, argon-plasma coagulation (APC) would be applied and a second SEMS would be considered only in case of a clear stenosis.

In case a second SEMS was necessary with the primary SEMS in situ, a minimum of 3 cm of overlap was attempted. Migrated stents were removed endoscopically; and if dysphagia persisted, a new stent was placed within 1-2 weeks. Patients with stents traversing the GEJ were prescribed proton pump inhibitors, and all patients were instructed, orally and in writing, to eat as close to normal food as possible, and to contact our department in case they encountered problems in swallowing.

Statistics

For comparison of paired categorical data, the Wilcoxon signed rank test was used. For continuous data, the Wilcoxon-Mann-Whitney rank sum was used. A p value < 0.05 was considered significant.

Trial registration: not relevant.

RESULTS

A total of 108 stents were inserted into 87 patients (63 males and 23 females) with a median age of 71 years (range: 41-94 years). Between them, 53 (60%) had adenocarcinomas, 25 (29%) had squamous-cell carcinomas, four (5%) had undifferentiated carcinomas and five (6%) patients were not histologically specified. The localization of the tumours were four (5%) in the upper oesophagus, 11 (13%) in the mid-oesophagus, 49 (56%) in the lower oesophagus and 23 (26%) in the GEJ.

The reasons for palliative treatment were: advanced (T4 and/or M1) disease at the time of diagnosis (n = 49), unfit for surgical treatment due to co-morbidity (n = 30), treated with SEMS due to luminal tumour recurrence (n = 5) or declined surgical treatment (n = 3). Fifty-two patients (60%) had been treated prior to stent placement with either palliative intent (n = 47) in the form of APC or with a curable intent (n = 5) in the form of radio-chemotherapy.

The primary stent was Ultraflex in 77 patients, seven patients had a Cook or Choo stent and three were treated with a Wallstent. For the 21 secondary stents, ten patients received covered Ultraflex stents, seven patients had a non-covered stent, and due to previous stent migration, four patients were treated with large-diameter stents (28 mm flange).

All but one SEMS were successfully placed, and no perforations occurred. In one case, the stent had to be dilated in order to expand fully. This stent later caused repeated incidents with food blockage, and it was therefore replaced and this patient encountered no further problems.

TABLE 1

Immediate (procedure-related) and late complications.

Complication	Patients, n (%)
Immediate (n = 1)	
Deaths	0
Perforation	0
Dislocation at placement	0
Technical stent failure	1 (1)
Late (n = 76)[a]	
Stent fracture	1 (1)
Dislocation of stent	11 (13)
Obstructing food	19 (22)
Tumour/tissue ingrowth	40 (46)
Bleeding	5 (6)

a) Some patients experienced more than one type of complication.

TABLE 2

Re-interventions.

Intervention	Procedures, n
Endoscopy with argon plasma coagulation	138
Endoscopy with other treatment[a]	82
New stent	21
Radiation therapy	2
Dilatation	1
Ethanol sclerotherapy	1

a) Balloon dilation, clearing of impacted food or food residues, etc.

Fifty (57%) patients had a dysphagia score documented in the patient record both before and after the stent insertion. The average score before and after stent insertion was 2.4 and 0.8, respectively ($p < 0.01$). None of these patients experienced an increase in dysphagia score after stenting, but the dysphagia score remained unchanged in two (4%) patients. In 39 (78%) patients, the dysphagia score was 0 or 1 after the placement of SEMS.

After the primary SEMS-placement, 60 patients (68%) experienced complications or dysphagia incidents that led to re-intervention (**Table 1**). There was no order or pattern in how these symptoms developed. The most common problem was tissue/tumour ingrowth (n = 40): Twenty-six had a problem at the proximal flange, 12 at the distal flange, and two patients had direct tumour growth through the body of the stent.

Seven patients (8%) experienced stent dislocation a total of 11 times. All stents had migrated to the stomach and all except one were retrieved endoscopically. One Wallstent had to be left in the stomach as further attempts of retrieval were deemed too risky. One SEMS was found to be fractured and was successfully replaced.

The above mentioned complications led to a total of 245 endoscopic re-interventions with an average of 2.8 per patient. The distribution of re-interventions is shown in **Figure 1**.

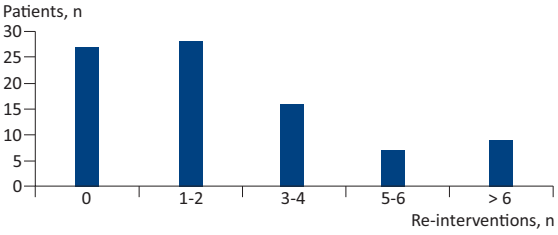
The overall median survival after the primary SEMS placement was 116 days (range 2-866 days). A total of 58 (67%) patients died within six months after stent-insertion. The average number of re-interventions was 1.5 in these patients, whereas it was 5.4 for patients who lived longer than six months ($p < 0.01$). The re-intervention rates were 0.5 re-interventions/month for patients surviving less than six months compared with 0.4 re-interventions/month ($p = 0.77$) for patients surviving more than six months after SEMS placement.

The most common re-intervention was APC of tumour/tissue ingrowth which was used in 138 cases (**Table 2**).

The median time from SEMS-placement to the first re-intervention was 44 days (range 2-438 days).

The 87 patients had a total of 251 hospital stays of which 245 were due to dysphagia or other SEMS-related complications. In 66 cases (27%), the re-interventions were carried out in an outpatient setting.

FIGURE 1



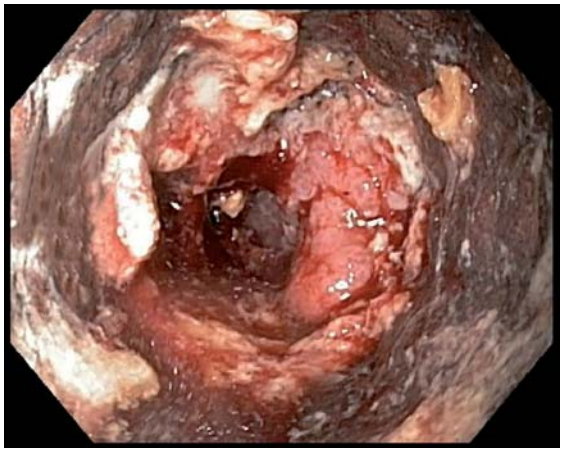
The distribution of re-interventions.

DISCUSSION

The procedure-related mortality and complication frequency in SEMS treatment are generally low [6, 8, 9]. We observed only one procedure-related complication (0.9%) due to incomplete stent expansion. This is very low compared with previous reports in which procedure-related complications ranged from 2.6% to 7.0% [6, 8, 9]. The fact that the majority of our patients had malignant obstruction in the lower part of the oesophagus (82%) may possibly explain this, since other studies have shown that complication rates and patient discomfort are generally higher in patients with upper oesophageal malignancies [10, 11]. Another reason may be the general use of one type of stent (Ultraflex) in the present study, which may allow us to become even more familiar with its properties and behavioural pattern. In addition, the relatively low expansive force of this stent [12] may also explain why we saw no perforations or bleedings.

A complete registration of the dysphagia score could be found in 57% of the patients. This is a major limiation of the retrospective design. However, as stated under Material and Methods, departmental guidelines regarding dysphagia and stent placement were followed, and there was no intentional selection in the registration of dysphagia score. For the patients with a complete registration of dysphagia before and after SEMS, the scores showed a significant reduction in dysphagia after stent insertion. This is in line with the litterature as other studies have found similar results that confirm the prompt relief of dysphagia after stent insertion [4].

We found that seven out of ten patients experienced late complications that warranted re-interventions, mainly because of recurrent dysphagia. The cause of this was tumour/tissue ingrowth, obstructing food and stent displacement, and the former two were also typical of non-SEMS treated disease. Our re-intervention rate was higher than the rates described in other studies, where they ranged from 22% to 50% [7, 8, 13-16]. This higher rate is not explained by a longer survival in our patients as this is comparable to similar studies [8, 9, 13, 15-17]. One might have expected this as our study showed that the number of interventions was significantly higher in the group of patients living more than six months than in the other group. However, the rate of interventions was the same in both groups. The expected number of re-interventions therefore seems to be dependent on the life-expectancy at the time of placement of the stent.



Tissue undergrowth leading to grade 3 dysphagia.

An explanation may be that our patients were instructed to eat normal food without any considerations, and also to contact our department directly in case of dysphagia. The fact that contact to a medical facility in Denmark has no economic consequences to the patient may also have led to a larger number of hospital visits, allthough none of the recorded contacts seemed unwarranted.

Tissue- or tumour growth were the most common complications. This seems to suggest that the longer the stent is in place the more tissue growth will be seen; hence, the longer time with the stent in situ, the more frequent the complications. APC was therefore the most frequent re-intervention modality in our study. In some instances, placing a second stent could have been an option, but when the stented area is lengthened, the motility is also reduced.

Lodged food was another frequent problem and this may be explained by the lack of food restrictions given to our patients. Maybe an increased focus on avoiding particular problematic foods and a change of eating habits would be required, but, on the other hand, patients express that the ability to eat normal food is an essential part of maintaining a reasonable quality of life.

Stent dislocation was seen 11 times and all migrated distally. All but one were removed endoscopically and subsequently replaced. Due to the problems with tumour/tissue ingrowth, covered stents are generally preferred, but it is also known that they tend to migrate more often [18]. To avoid migration, the use of larger diameter stents seems tempting, but studies have shown that these may cause even more complications [19].

The survival after SEMS placement was quite short (mean 116 days) which emphazises the need for quick relief of dysphagia rather than a more prolonged effect. However, the range in survival was wide (2-866 days), and a different strategy may be needed in patients with a longer remaining life expectancy. There is some evidence that brachytherapy provides more effective dysphagia relief in the period from 6 to 12 months after palliation [3, 4], and this procedure should be considered for these patients. The ability to distinguish between patients with short and long lifespan, respectively, is a key question in the palliative setting. The identification and validation of prognostic factors was beyond the scope of the current study. Besides prognostic factors, the impact on quality of life (QoL) after SEMS or other local treatments is important when choosing between treatment modalities, especially since there is a high rate of re-interventions. We did not register QoL in the present study, but the high rate of re-interventions has motivated the initiation of a larger prospective study that includes QoL. It remains unknown whether the longer lifespan and the ability to suspend the need for immediate relief of dysphagia are associated with a lower degree and slower rate of disease progression at the time of palliation. The generally short expected lifespan calls for immediate relief of dysphagia, and this makes SEMS an obvious choice.

In conclussion, SEMS treatment was a safe and effective palliation of malignant obstruction in the oesophagus and GEJ region, but the procedure was associated with a frequent need for re-intervention. Ongoing research in this area is therefore necessary, and this study has given rise to the initiation of a prospective study, which is currently in progress, in order to examine some of the questions to which this study has given rise.

CORRESPONDENCE: *Ole Steen Bjerring*, Aarestrupvej 25, 5230 Odense M, Denmark. E-mail: steenbjerring@gmail.com

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CONFLICTS OF INTEREST: none

LITERATURE

1. Sagar PM, Gauperaa T, Sue-Ling H et al. An audit of the treatment of cancer of the oesophagus. Gut 1994;35:941-5.
2. Watt E, Whyte F. The experience of dysphagia and its effect on the quality of life of patients with oesophageal cancer. Eur J Cancer Care (Engl) 2003;12:183-93.
3. Sreedharan A, Harris K, Crellin A et al. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev 2009;(4th issue): CD005048.
4. Bergquist H, Wenger U, Johnsson E et al. Stent insertion or endoluminal brachytherapy as palliation of patients with advanced cancer of the esophagus and gastroesophageal junction. Results of a randomized, controlled clinical trial. Dis Esophagus 2005;18:131-9.
5. O'Donnell CA, Fullarton GM, Watt E et al. Randomized clinical trial comparing self-expanding metallic stents with plastic endoprostheses in the palliation of oesophageal cancer. Br J Surg 2002;89:985-92.
6. Wengrower D, Fiorini A, Valero J et al. EsophaCoil: long-term results in 81 patients. Gastrointest Endosc 1998;48:376-82.
7. Knyrim K, Wagner HJ, Bethge N et al. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med 1993;329:1302-7.
8. Christie NA, Buenaventura PO, Fernando HC et al. Results of expandable metal stents for malignant esophageal obstruction in 100 patients: short-term and long-term follow-up. Ann Thorac Surg 2001;71:1797-801.
9. Golder M, Tekkis PP, Kennedy C et al. Chest pain following oesophageal stenting for malignant dysphagia. Clin Radiol 2001;56:202-5.
10. Kawasaki R, Sano A, Matsumoto S. Long-term outcomes and complications of metallic stents for malignant esophageal stenoses. Kobe J Med Sci 2003;49:133-42.
11. Choi EK, Song HY, Kim JW et al. Covered metallic stent placement in the management of cervical esophageal strictures. J Vasc Interv Radiol 2007;18:888-95.
12. Chan AC, Shin FG, Lam YH et al. A comparison study on physical properties

of self-expandable esophageal metal stents. Gastrointest Endosc 1999;49:462-5.
13. Bartelsman JF, Bruno MJ, Jensema AJ et al. Palliation of patients with esophagogastric neoplasms by insertion of a covered expandable modified Gianturco-Z endoprosthesis: experiences in 153 patients. Gastrointest Endosc 2000;51:134-8.
14. Homs MY, Steyerberg EW, Kuipers EJ et al. Causes and treatment of recurrent dysphagia after self-expanding metal stent placement for palliation of esophageal carcinoma. Endoscopy 2004;36:880-6.
15. De Palma GD, di ME, Romano G et al. Plastic prosthesis versus expandable metal stents for palliation of inoperable esophageal thoracic carcinoma: a controlled prospective study. Gastrointest Endosc 1996;43:478-82.
16. Kozarek RA, Raltz S, Brugge WR et al. Prospective multicenter trial of esophageal Z-stent placement for malignant dysphagia and tracheoesophageal fistula. Gastrointest Endosc 1996;44:562-7.
17. Gray RT, O'Donnell ME, Scott RD et al. Self-expanding metal stent insertion for inoperable esophageal carcinoma in Belfast: an audit of outcomes and literature review. Dis Esophagus 2011;24:569-74.
18. Uitdehaag MJ, van Hooft JE, Verschuur EM et al. A fully-covered stent (Alimaxx-E) for the palliation of malignant dysphagia: a prospective follow-up study. Gastrointest Endosc 2009;70:1082-9.
19. Harbord M, Dawes RF, Barr H et al. Palliation of patients with dysphagia due to advanced esophageal cancer by endoscopic injection of cisplatin/epinephrine injectable gel. Gastrointest Endosc 2002;56:644-51.