

A new fully covered stent with antimigration properties for the palliation of malignant dysphagia: a prospective cohort study

Madeleen J. Uitdehaag, RN, MSc, Peter D. Siersema, MD, PhD, Manon C. W. Spaander, MD, MSc, Frank P. Vleggaar, MD, PhD, Els M. L. Verschuur, RN, PhD, Ewout W. Steyerberg, PhD, Ernst J. Kuipers, MD, PhD

Rotterdam, Utrecht, The Netherlands

Background: Fully covered stents are designed to resist tissue ingrowth that is often seen with partially covered stents. An issue with fully covered stents is the risk of migration.

Objective: We aimed to determine efficacy, recurrent dysphagia, and complications of the SX-ELLA stent Esophageal HV, which is fully covered to resist tissue ingrowth and has an antimigration ring to withstand migration.

Design: Prospective cohort study.

Setting: Two tertiary referral centers.

Patients: Forty-four patients with malignant esophageal strictures from inoperable or metastatic esophageal or gastric cardia cancer (n = 42) or lung cancer (n = 2).

Interventions: Placement of an SX-ELLA stent.

Main outcome measures: Functional outcome, recurrent dysphagia, complications, and survival.

Results: Dysphagia improved from a median score of 3 (liquids only) before stent placement to 1 (ability to eat some solid food) 4 weeks later ($P < .001$). Twelve of 44 (Kaplan Meier analysis = 40%) patients developed 18 episodes of recurrent dysphagia of which 6 were caused by stent migration and 2 by tissue overgrowth. In total, 14 episodes of major complications developed in 10 of 44 (Kaplan Meier analysis = 29%) patients, 8 of which were caused by hemorrhage. After a median follow-up of 15 months, 39 patients had died (median survival 110 days), 5 (11%) from hemorrhage.

Limitations: Nonrandomized study design.

Conclusions: Dysphagia caused by esophageal cancer can be successfully palliated by placement of a new, fully covered esophageal stent (SX-ELLA). Although this single-wire braided stent with an antimigration ring is supposed to be less traumatic and to reduce migration, this was not substantiated in this study. Further improvements of stent features are needed to achieve the goals set for this study.

Metal stents have become popular for the palliation of patients with malignant esophageal obstruction, especially patients with a poor prognosis.^{1,2} Initially, most stents were partially covered. These stents have as a major disadvantage that recurrent dysphagia caused by tumoral and

nontumoral tissue growth through the uncovered stent mesh frequently occurs.³⁻⁸ In the past few years, fully covered stents have been introduced. Although the full covering of these stents prevents tissue ingrowth, the issues of both tissue overgrowth and stent migration remain.⁴⁻⁹

Recently, a new stent, the SX-ELLA stent Esophageal HV (Ella-CS, Hradec Kralove, Czech Republic), was developed for the palliation of malignant dysphagia. This stent (Fig. 1) is made of a nickel-titanium alloy (nitinol) and is braided from 1 piece of wire that should make the stent ends less traumatic and improve the flexibility of the stent with expected reduced hyperplastic (nontumoral) tissue overgrowth.¹⁰ To decrease the risk of migration, the SX-

Abbreviations: IQR, interquartile range; KM, Kaplan-Meier.

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Figure 1. The fully covered SX-ELLA stent with an antimigration ring at the upper stent end.

ELLA stent has a flip-flop type of antimigration ring that is circumferentially attached to the proximal stent portion (Fig. 2). This ring functions as a circular hook preventing migration, but is also flexible and is everting when the traction force is too strong. This mechanism should reduce the risk of esophageal wall injury. The stent flares to 25 mm at its proximal and distal ends with a body diameter of 20 mm.

The aim of this study was to determine the efficacy of the SX-ELLA stent for the palliation of malignant dysphagia in patients with inoperable or metastatic esophageal, gastric cardia, or lung cancer, with special emphasis on recurrent dysphagia particularly caused by tissue overgrowth and migration.

METHODS

Patients

Between February 2007 and May 2008, 45 patients with dysphagia caused by esophageal, gastric cardia, or lung cancer were consecutively enrolled in the study. Inclusion criteria were inoperable malignant obstruction of the esophagus or gastric cardia caused by esophageal, cardia, or lung carcinoma. All patients gave written informed consent. Exclusion criteria were an obstruction length of

Capsule Summary

What is already known on this topic

- Fully covered esophageal stents prevent tissue ingrowth, but tissue overgrowth and stent migration may still occur.

What this study adds to our knowledge

- In a prospective study of 44 patients with malignant esophageal strictures who underwent placement of fully covered, single-wire braided stents, dysphagia scores improved, but major complications developed in 10 patients, including stent migration and hemorrhage.

more than 12 cm, tumor growth within 2 cm of the upper esophageal sphincter, and a fistula between the esophagus and respiratory tree. Patients who were unfit to undergo conscious sedation were also excluded. Stent placement was performed at 2 tertiary referral hospitals, the Erasmus MC–University Medical Center Rotterdam and the University Medical Center Utrecht, both in The Netherlands. The medical ethics committees of both hospitals approved the study.

Methods

All patients were evaluated before stent placement and at 4-week intervals after stent placement until death. Evaluations were performed by scheduled telephone calls to each patient and/or the patient's general practitioner and included the ability to eat and/or swallow (graded as follows: 0 = ability to eat a normal diet, 1 = ability to eat some solid food, 2 = ability to eat some semisolids only, 3 = ability to swallow liquids only, and 4 = complete dysphagia)¹¹ and specific symptoms such as pain, heartburn, and weight loss. In cases of recurrent dysphagia or complications, patients were seen for evaluation and/or treatment. When a patient was referred to another hospital, relevant clinical information was obtained.

Stent placement

All patients were consciously sedated with midazolam (Dormicum; Roche Nederland BV, Mijdrecht, The Netherlands) during stent insertion. If indicated, the stricture was first dilated to 9 to 10 mm by using Savary dilation or (preferably) a small-caliber (5.9 mm) endoscope (Olympus BV, Zoeterwoude, The Netherlands) to allow the tumor to be inspected, the tumor margins to be marked, and a guidewire to be placed. A stent measuring 2 to 4 cm longer than the stricture was chosen to allow for a 1- to 2-cm extension above and below the proximal and distal tumor shoulder.

Statistical analysis

The results were expressed as mean \pm standard deviation and medians and interquartile range (IQR); survival



Figure 2. The antimigration ring of the SX-ELLA stent showing its flip-flop mechanism to prevent migration.

was expressed as median survival. Differences in dysphagia score before and 1, 3, and 6 months after treatment were analyzed by the Wilcoxon rank-sum test. The percentages of patients with complications and recurrent dysphagia were calculated by using the Kaplan-Meier (KM) method to adjust for time of occurrence of the event and survival differences.

RESULTS

Functional outcome

Successful placement of 46 SX-ELLA stents was achieved in all 45 patients. Because 1 patient was lost to follow-up, clinical characteristics of 44 patients are shown in Table 1. In all 25 (57%) patients with a tumor located in the distal esophagus or gastric cardia, the stent crossed the gastroesophageal junction. Eight patients died before the 4-week follow-up, with 1 of them having symptoms of hemorrhage and upper abdominal pain that were considered to be related to stent insertion. After 4 weeks, the

TABLE 1. Characteristics of 44 patients treated with an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer

	Total (N = 44)
Age, y, mean \pm SD	64 \pm 11
Male sex, no. patients (%)	35 (80)
Dysphagia score before treatment, median (IQR)	3 (1)
WHO performance score before treatment (IQR)	1 (1)
Tumor length, cm, mean \pm SD	6.8 \pm 3.8
Tumor location, no. patients (%)	
Proximal or mid esophagus	17 (39)
Distal esophagus or gastric cardia	25 (57)
Lung	2 (5)
Histology, no. patients (%)	
Squamous cell carcinoma	19 (43)
Adenocarcinoma	24 (55)
Unknown	1 (2)
Previous radiation and/or chemotherapy, no. patients (%)	
Chemotherapy	9 (21)
Radiation	3 (7)
Radiation and chemotherapy	6 (14)
Dilation before treatment, no. patients (%)	4 (9)

SD, Standard deviation; IQR, interquartile range; WHO, world health organization.

dysphagia had improved from a median score of 3 to 1 ($P < .001$). This persisted in patients who were still alive after 3 and 6 months (Fig. 3).

Recurrent dysphagia

In total, 18 episodes of recurrent dysphagia developed in 12 of 44 (KM = 40%) patients with an SX-ELLA stent, which were caused by food impaction (8 episodes), stent migration (6 episodes), tumor overgrowth (2 episodes), stent fracture (1 episode), and an incomplete deployed distal part of the stent (1 episode) (Table 2). Three patients had more than 1 episode of recurrent dysphagia.

Complications

In total, major and minor complications were seen in 18 of 44 (KM = 47%) patients (Table 2). Of these, 14 major complications occurred in 10 patients (KM = 29%), including hemorrhage ($n = 8$), severe pain ($n = 3$), fistula formation ($n = 2$), and fever ($n = 1$). Of the 7 patients with hemorrhage, it developed in 1 patient within 7 days of stent

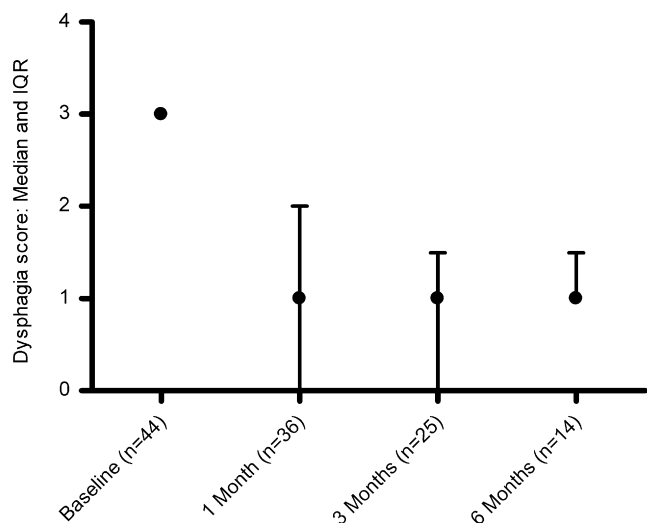


Figure 3. Median dysphagia score over time after placement of an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer.

placement, whereas another patient had 2 episodes of hematemesis 43 and 84 days after stent placement. Five patients eventually died of this complication, and 2 patients were successfully treated with radiation therapy.

Minor complications were seen in 12 patients (KM = 30%; Table 2). Of these patients, 5 experienced gastroesophageal reflux symptoms after a median of 5 days (IQR 2-55 days) and 7 patients experienced mild retrosternal pain after a median of 6 days (IQR 3-14 days).

Survival

After a median follow-up of 15 months (IQR 11-19 months), 39 (89%) of 44 patients had died, resulting in a median survival of 110 days (95% CI, 95-180 days). Five patients died of hemorrhage 5, 43, 107, 128, and 248 days after stent placement, respectively.

DISCUSSION

In this prospective follow-up study of 44 patients, we demonstrated that the SX-ELLA stent provided good symptomatic relief of malignant dysphagia. In addition, we found a low rate of tissue overgrowth (KM = 8%), but a similar frequency of stent migration (KM = 20%), as previously reported with other expandable stents.^{1,9,12-21} In addition, despite the single-wire, braided, low-trauma design, the frequency of hemorrhage and fistula formation was considerable with this stent. This was particularly true for hemorrhage (KM = 25% after 7 days), which was fatal in 5 patients (Table 2).

The frequency of tumoral or nontumoral tissue overgrowth was reduced with the SX-ELLA stent (2 episodes in 2 patients, KM = 8%) compared with rates of tissue ingrowth and overgrowth with other stent designs

TABLE 2. Recurrent dysphagia and complications after placement of an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer

	Total (N = 44)
Recurrent dysphagia (%)*	18 episodes in 12 pts (27-40)*
Stent migration	6 episodes in 6 pts (14-20)
Overgrowth	2 episodes in 2 pts (5-8)
Food impaction	8 episodes in 5 pts (11-17)
Other	2 episodes in 2 pts† (5-9)
Total no. complications (%)	26 complications in 18 pts (41-47)
No. major complications	14 complications in 10 pts (23-29)
≤ 7 days	
Severe pain	3 in 3 pts (7-7)
Hemorrhage	1 (2-2)
Fever	1 (2-2)
< 7 days	
Hemorrhage	7 in 6 pts (14-25)
Fistula	2 in 2 pts (5-6)
Minor complications	12 in 12 pts (27-30)
Mild pain	7 in 7 pts (16-16)
Gastroesophageal reflux	5 in 5 pts (11-13)

*% = valid percentage versus percentage measured by the Kaplan-Meier method (6 months), respectively.
 †Stent not fully deployed (1 patient) and stent fracture (1 patient).

(Table 3).^{1,9,12-21} It is not clear what the predominant reason for the low rate of tissue ingrowth and overgrowth was with the SX-ELLA stent. Fully covered stents have been designed to prevent tissue ingrowth, but this advantage may be outweighed by the still high rate of tissue overgrowth over the edge of these stents. Mayoral et al¹⁰ were the first to report nonmalignant tissue ingrowth and overgrowth as a cause of recurrent dysphagia in 47% of patients after stent placement for an esophageal malignancy. The larger size of the mid portion of the SX-ELLA stent (20 mm) compared with the Polyflex, Niti-S, and Gianturco Z stent (all 18 mm) could be a factor in the relatively low overgrowth rate. Verschuur et al¹⁵ found that large-diameter stents reduced the risk of recurrent dysphagia from tissue overgrowth. They suggested that this was because of the fact that a longer time is required to obstruct the esophagus when larger-diameter stents are placed. Furthermore, the braiding of the stent from 1 piece of wire could also prevent nonmalignant tissue overgrowth to occur by making both stent ends cause less trauma.

TABLE 3. Recurrent dysphagia and major complications after stent placement of partially or fully covered stents for the palliation of malignant dysphagia in other recently published series

Author/year	Intervention	Covering	No.	No. patients (valid %)			
				Recurrent dysphagia		Major complications (hemorrhage, fistula, fever, severe pain, perforation, aspiration pneumonia)	
				Tumoral/ nontumoral overgrowth	Migration	Total reported	Hemorrhage
Randomized trials							
Verschuur et al, 2008 ¹⁶	Ultraflex stent	Partial	42	13 (31)	7 (17)	9 (21)	5 (12)
	Niti-S stent	Complete*	42	10 (24)	5 (12)	5 (12)	2 (5)
	Polyflex stent	Complete	41	4 (10)	12 (29)	8 (20)	5 (12)
Conio et al, 2007 ⁹	Ultraflex stent	Partial	54	14 (26)	2 (4)	3 (6)	0
	Polyflex stent	Complete	46	14 (30)	6 (13)	4 (9)	2 (4)
Homs et al, 2004 ¹	Ultraflex stent	Partial	108	16 (15)	18 (17)	27 (25)	14 (13)
	Brachytherapy	-	101	-	-	-	-
Sabharwal et al, 2003 ¹⁴	Ultraflex stent	Partial	31	1 (3)	2 (6)	3 (10)	1 (3)
	Flamingo wallstent	Partial	22	1 (5)	1 (5)	3 (14)	1 (5)
Comparative studies							
Verschuur et al, 2007 ^{15,†}	Ultraflex stent	Partial	153	20 (13)	27 (18)	38 (25)	23 (15)
	Flamingo Wallstent	Partial	96	16 (17)	8 (8)	18 (19)	8 (8)
	Gianturco Z stent	Complete	89	16 (18)	5 (6)	20 (22)	13 (15)
Homs et al, 2004 ¹⁷	Ultraflex stent	Partial	75	7 (9)‡	17 (23)‡	NR	NR
	Flamingo wallstent	Partial	71	12 (17)‡	5 (7)‡	NR	NR
	Gianturco Z stent	Complete	70	11 (16)‡	4 (6)‡	NR	NR
Prospective studies							
Uitdehaag et al, 2008 ¹⁸	Alimaxx-E stent	Complete	45	7 (16)	16 (36)	9 (20)	2 (4)
Conigliaro et al, 2007 ¹²	Polyflex stent	Complete	60	8 (14)	12 (20)	NR (10)	4 (7)
Szegedi et al, 2006 ¹⁹	Polyflex stent	Complete	69	9 (13)	3 (5)	0	0
Verschuur et al, 2006 ²⁰	Niti-S stent	Complete*	42	2 (5)	3 (7)	5 (12)	2 (5)
Dormann et al, 2003 ²¹	Polyflex stent	Complete	33	4 (12)	2 (6)	0	NR
Retrospective studies							
Ross et al, 2007 ¹³	Wallstent II	Partial	97	5 (5)	5 (5)	17 (18)	14 (14)

NR, Not reported.
 *Inner fully covered with outer uncovered wire tube.
 †Small- and large-diameter stents are counted as 1 group.
 ‡Number of events rather than number of patients.

The use of SX-ELLA stents did not reduce the migration rate (6 episodes in 6 patients, KM = 20%) compared with migration rates found in other fully covered stent designs (Table 3).^{9,12,15-18} This suggests that the circumferential antimigration ring plus the flared ends are not sufficiently effective in preventing migration. The fact that 40% of the patients still experienced an episode of re-

current dysphagia was also caused by a relative high food obstruction rate, ie, 8 episodes in 5 patients (KM = 17%). Food obstruction occurred in 4 of 5 patients 9 to 33 days after placement, with 1 patient even experiencing 3 episodes. The cause of food obstruction was not clear because all patients received specific dietary advice. It may well be, however, that the metal retrieval iron loop played

a role because it was the obvious cause in at least 1 of the patients.

The SX-ELLA stent was associated with a considerable rate of major complications, with 14 occurring in 10 patients in this study. Of these, 7 patients experienced 8 episodes of hemorrhage. Until now, this is the highest hemorrhage rate observed with large-diameter stents as reported in the literature (Table 3).^{1,9,12-16,18,22} We speculate that the antimigration ring of the SX-ELLA stent was involved because not only hemorrhage, but also severe pain (n = 3) and fistula formation at the upper end of the stent (n = 2) were observed. In normal circumstances, stents exert some pressure on the tumor and the normal mucosa of the esophagus to affix the stent to the esophageal wall to reduce migration risk. With the SX-ELLA stent, this effect may be more pronounced because of the pressure effect of the antimigration ring, particularly when it is flipping in and out for its antimigration effect. In addition, specific stent characteristics, particularly stent diameter and radial force, should be taken into consideration. As mentioned previously, the relatively large mid section of the SX-ELLA stent could also increase the risk of hemorrhage, as has been reported previously.¹⁵ In conclusion, the SX-ELLA stent provided good symptomatic relief of malignant dysphagia with a low rate of tissue overgrowth. Migration rates occurred, however, at a similar (high) frequency as that observed with other currently available fully covered stents. In addition, a relatively high complication rate, particularly hemorrhage, was observed. It remains to be established whether friction from the antimigration ring or the large size of the mid section of the stent increased the risk of injury to the esophageal wall.

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Current affiliations: Departments of Gastroenterology and Hepatology (M.J.U., P.D.S., M.C.W.S., E.M.L.V., E.J.K.), Public Health (E.W.S.), and Internal Medicine (E.J.K.), Erasmus MC-University Medical Center Rotterdam, Rotterdam, The Netherlands, Utrecht Palliative Care Center (M.J.U., F.P.V.) and Department of Gastroenterology and Hepatology (P.D.S.), University Medical Center Utrecht, Utrecht, The Netherlands, Association of Comprehensive Cancer Centers (M.J.U.), Utrecht, The Netherlands.

Reprint requests: M.J. Uitdehaag, RN, MSc, Association of Comprehensive Cancer Centers, Postbus 19001, 3501 DA, Utrecht, The Netherlands.