Self-expanding stents in oesophageal cancer

Guido Costamagna, Michele Marchese and Federico Iacopini

- **The overall prognosis of patients with inoperable oesophageal cancer is poor. Palliative therapy for dysphagia is the only therapeutic concern for most patients.**
- **Self-expandable metal stents have several advantages over the other palliative methods as they are easy to use, do not require predilation and give rapid relief from dysphagia and a low complication rate.**
- **The various models of self-expandable metal stents, different in the flexibility, size and presence or absence of a coverage, permit to adapt the stent to the features of the stricture and the presence of fistulae. Metal stents can be, however, difficult to remove and have high initial costs.**
- **Self-expandable plastic stents are easily retrievable and inexpensive and seem to achieve good palliative results in oesophageal neoplasms. There are, however, some limitations: significant stricture dilation is necessary before stent placement and angulated strictures are difficult to negotiate owing to the stiff and large delivery catheter. Furthermore, the complete coverage of the stent may represent a risk factor in early and late stent migration.**

The main therapeutic concern in patients with inoperable oesophageal cancer is palliation of dysphagia. Self-expandable metal stents are widely used because they are safer than conventional plastic stents, offer rapid relief from dysphagia and may seal off tracheo-oesophageal fistulae. Self-expanding metal stents, particularly when uncovered, are, however, associated with the disadvantage of tumour ingrowth. Self-expandable plastic stents are entirely covered and easy to reposition in case of migration and usually induce less inflammatory proliferation at their flanges when compared with metal stents. The major disadvantage of the current version of plastic stents is the large diameter and stiffness of the stent delivery system when compared with metal stents. Therefore, plastic stents are more difficult to place in patients with angulated strictures or with tumours located in the cervical oesophagus near the upper sphincter. ***Eur J Gastroenterol Hepatol*** **18:1177–1180 © 2006 Lippincott Williams & Wilkins.**

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Introduction

Patients with dysphagia as a consequence of oesophageal cancers can be radically treated in less than 50% of cases because of the metastatic spread or locally advanced disease with a survival of less than 20% at 12 months [1], and in 10–15% of cases because they are unfit for surgery. Therefore, the main therapeutic target for advanced oesophageal cancer is palliation for the relief of dysphagia, maintenance of nutrition and improving the patient's quality of life. There are numerous nonsurgical treatment modalities to provide palliation for dysphagia, which include endoscopic tumour ablation and stenting, radiation therapy and chemotherapy. The ideal palliation should be rapid, well tolerated, long-lasting and preferably performed as an outpatient procedure and at low costs. Endoscopic ablative methods, that is, thermal, photochemical or photodynamic therapy or the injection of sclerosants or cytotoxic agents, require multiple sessions both to obtain and maintain the patency with dramatic effects on the quality of life. Currently, the recommended approaches are placement of self-expandable stents and/or radio-chemotherapy.

Self-expandable metal stents

Oesophageal endoprostheses have undergone a remarkable technological evolution since the rigid plastic stents which were associated with high complication rates. The concept of self-expandable metal stents (SEMS) is of a tube compressed and restrained in a delivery device of much smaller diameter. These devices can be safely introduced through a tumour without predilation during an outpatient procedure under conscious sedation. SEMS can be mainly differentiated from the material they are made of (stainless steel and nitinol, a shaped memory alloy of nickel and titanium), and on the presence of a plastic coverage fully or partially covering the mesh. SEMS also, however, differ in shape, diameter and type of delivery system. Stainless-steel models are the Wallstent Esophageal II (Microvasive/Boston Scientific, Natick,

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Massachusetts, USA) and the Z-stent (Cook Endoscopy, Winston Salem, North Carolina, USA). Wallstent consists of a braided mesh partially covered stent. The shaft diameter is 18 or 22 mm, flaring to 28 mm and it comes in lengths of 10 and 15 cm. The endoprosthesis is premounted on an 18F catheter resheathable delivery system and undergoes a 20–25% longitudinal shortening on deployment. The Flamingo Wallstent is a conic-shaped covered stent developed to overcome the high rate of distal migration of stents placed in the oesophago-gastric region. The Z-stent consists of an entirely or partially covered stent configured into 2-cm zigzag-shaped segments attached consecutively. The stent comes in lengths of 6, 8, 10, 12 and 14 cm and two shaft diameters, 18 mm flared to 21 mm or 25 mm flared to 27 mm. This stent is compressed into a 28F catheter delivery system and does not shorten on deployment.

Nitinol stents are the Ultraflex Esophageal Stent (Microvasive/Boston Scientific), the Choostent (M.I. Tech Co., Seoul, Korea), and the Niti-S (Taewoong Medical Inc., Kyunggi-Do, Korea) stents. The Ultraflex has a flared proximal end (23 or 28 mm) and the covered versions have 1.5 cm of bare nitinol without sharp elements at both sides. This stent is highly flexible and is released from a 20F delivery system by pulling a suture string. Moreover, it can be deployed by distal or proximal release mechanisms under endoscopic visualization. Choo-stent and Niti-S are both fully covered and differ from Ultraflex in the angulation between the body and the flanges.

Currently, endoscopic placement of SEMS is the quickest method for palliation of dysphagia for patients with inoperable and/or unresectable malignant oesophageal strictures, for occlusion of malignant oesophago-respiratory fistulae and also for recurrent malignant strictures after oesophago-gastric resection [2–6]. When compared with rigid plastic stents, patients palliated with SEMS have a similar survival rate, a lower incidence of acute insertional complications, that is, perforation, and a significant reduction of the mortality rate, as shown in a recent review of 1238 patients [7]. The technical and clinical success of palliation with SEMS is more than 95% (range 85–100%), although up to 22% of patients require a second prosthesis at the time of initial placement [8].

Once deployed, covered and uncovered SEMS are associated with different complications. Malfunction of uncovered SEMS is mainly related to ingrowth and overgrowth in 17–30 and 9%, respectively [9,10]. In patients with a prolonged survival, the use of covered SEMS permits to significantly reduce the incidence of ingrowth (3%) and the need for additional endoscopic intervention to restore patency. Owing to an insufficient anchorage of the metallic mesh to the oesophageal wall however, both partially and fully covered SEMS have a higher risk of migration (15 and 35%, respectively) than uncovered stents (7%) [9–11]. Although concerns have been raised about the possibility to position stents in proximal oesophageal neoplasms, the clinical success rate of SEMS in the cervical region is similar to that in the mid/distal thirds of the oesophagus, without an increased risk of perforation, pulmonary aspiration and migration into the hypopharynx. The upper limit from the proximal end of the stent to the upper oesophageal sphincter should be 2 cm because data from the literature show that an intolerable foreign body sensation was reported in 28% of patients when SEMS were placed up to 1.5 cm from the upper oesophageal sphincter and by none when the proximal limit was 2 cm [12,13]. The feared airway obstruction or compression secondary to SEMS placement into the proximal or mid-oesophagus can be assessed preoperatively by bronchoscopy or leaving a dilator in place for 30–60 s to assess respiratory compromise owing to tumour displacement. If such a compromise occurs, oesophageal stent placement should be preceded by tracheal stenting [14].

The availability of a wide selection of SEMS allows to choose the stent according to the characteristics of each stricture. Covered SEMS are mandatory to treat oesophageal cancer complicated with tracheo-oesophageal fistula. Resolution of symptoms is achieved in 70–100% of cases and the complication rate is similar to that in patients without fistulae [15,16]. Large calibre stents (28–30 mm), such as the Flamingo Wallstent, are generally used at the distal oesophagus and at the oesophago-gastric junction to reduce migration rate without an increase of complications [2]. Finally, SEMS with antireflux valves are available to prevent the gastro-oesophageal reflux disease when stenting involves the oesophageal-gastric junction [17]. No sufficient data, however, exist to demonstrate whether antireflux SEMS can prevent gastro-oesophageal reflux disease without compromising food passage [18] and if they are cost-effective against the use of proton pump inhibitors [7].

Self-expandable plastic stents

Self-expandable plastic stents (SEPS) have been developed to overcome SEMS drawbacks such as the difficulty of adjusting the stent position and removal, and initial high costs [10]. The only commercially available model is Polyflex (Microvasive/Boston Scientific), a woven polyester stent entirely covered by a silicone membrane. The proximal end is slightly flared, whereas the middle and distal portions of the stent have the same diameter (small 16 mm; medium 18 mm; large 21 mm). The stent is available in three stent lengths: 9, 12 and 15 cm, and each one is available in all three diameters. This stent has a high malleability permitting an easy and atraumatic repositioning or removal, but also a sufficient radial force

Table 1 Outcomes of Polyflex placement for oesophageal malignant strictures

Authors	No. of patients	Technical success		Follow-up, mean (months)	Migration (oesophageal location)	Overall complications
		%	Mechanical dilation			
Bethge and Vakil [21]	8	100	NA	3	1/8 (cardia)	1 (fistula after radiotherapy)
Decker *et al.* [22]	14	100	14/14	6	1/14	2/14 (overgrowth)
Costamagna *et al.* [24]	14	86	10/14	3	2/12 (cardia, mid-portion)	1/12 (overgrowth)
Dormann *et al.* [23]	33	100	5/33	5	2/33 (cardia)	4/33 (overgrowth) 1/33 (food impaction)
Szegedi *et al.* [26]	69	96	31/66	4	3/66	9/66 (overgrowth) 2 (fistula)

to restore luminal patency and remain anchored firmly to the tumour. According to these features, some groups proposed their temporary use for refractory benign oesophageal strictures and anastomotic leaks [19,20].

Data on clinical efficacy of SEPS in malignant oesophageal strictures are extremely limited (Table 1). First studies [21,22] reported a successful placement of SEPS associated with a significant improvement of dysphagia in all cases. Migration occurred in 6% of cases however, most frequently when placed at the oesophago-gastric junction (two out of six patients) [23].

Our preliminary experience with SEPS in 16 patients with inoperable oesophageal strictures has been quite satisfactory [24]. Successful placement was possible in 86% of patients with a neoplastic stricture, and distal migration occurred in 16% of cases within a 3-month follow-up. The high migration rate in our study may be related to the great proportion of patients with malignant recurrence at the surgical anastomosis or at the oesophago-gastric junction (64%). Moreover, one SEPS placed at the mid-portion of the oesophagus probably migrated after radiotherapy.

Currently, SEPS have some disadvantages vs. SEMS. Stents need to be loaded into a delivery device that can be awkward to assemble, has a very large diameter (36–42F vs. 16–28F of SEMS) and high rigidity, and a short nonflexible conic tip at the distal end. These features increase the difficulty of SEPS placement. The rigidity of the system requires to hyperextend the patient neck, to use stiff guide-wires and may increase the risk of perforation, particularly in angulated strictures or tumour location in the proximal oesophagus. Moreover, the large calibre of the catheter may require an aggressive preplacement stricture dilation (Table 1) that is associated with a risk of oesophageal perforation in 8–13% of cases and bleeding or fistula formation in 5–10%, respectively [1,25]. In our experience, the placement of SEPS was not possible in 25% of cases because of failure to pass the delivery device through the stricture despite a 14 mm mechanical dilation and a failure of the stent to open despite correct deployment in one case [24]. Finally, SEPS may retract up to 30% of their length and are consequently more difficult to place than SEMS [22]. This disadvantage is partly counterbalanced by the possibility of correcting the position during stent release.

The report by Szegedi *et al.* [26] in this issue of the journal comprising 69 patients with advanced oesophageal cancer treated with SEPS is the largest available series. Mechanical dilation was necessary to pass the delivery catheter in 47% of the cases, but technically failed in three cases out of the seven proximal malignant strictures. Dysphagia improved significantly within 1 week without major complications and migration was limited to stents placed at the distal third of the oesophagus or at the oesophago-gastric junction. A 15% migration rate was observed for SEPS at the oesophago-gastric junction, although the stent was routinely fixed to the mucosa with an endoclip. Unfortunately, the authors do not show data regarding the migration rates related to the various lengths and diameters of SEPS and tumour location. According to literature data, it does not seem that SEPS migrate more frequently than SEMS in malignant oesophageal strictures and, in our opinion, this probability could be further reduced by using larger stents or converting the full coverage into a coverage limited at the mid-portion.

Conclusions

Nowadays endoscopic treatment can adequately palliate dysphagia secondary to almost all malignant oesophageal strictures. This is achieved by expertise and a selection of the stent (type, length, size and delivery system) tailored on the stricture features and the patient condition. Endoscopic stenting, however, gives the best clinical results in the short-term follow-up, and chemotherapy and/or radiotherapy (CRT) should be preferred when survival is prolonged, although palliation of dysphagia is delayed for almost 1 month. In a recent study, in fact, a single-dose brachytherapy provided a greater relief of dysphagia with fewer complications (late haemorrhages, migration and perforations), reducing the need of retreatment in the long term than SEMS [27]. Although the relationship between endoscopic treatment and CRT is still unclear, SEMS palliation can be safely performed after an incomplete result of CRT [28]. On the contrary, SEMS placement should be avoided in patients who will

undergo CRT, as tumour shrinkage may increase the chance of stent migration and the risk of severe complications. In patients with severe dysphagia, a temporary percutaneous endoscopic gastrostomy could be the recommended method for nutrition, although SEPS, which can be easily removed, may represent an alternative treatment with an improvement in the patient's quality of life.

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