

Esophageal Stenting in Patients with Advanced Esophageal Cancer

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Editor's Note: Due to production constraints, Figures 1-6 are not printed in the journal. They are available online at www.dcmsonline.org as web illustrations.

Abstract: *Esophageal carcinoma is a common cause of cancer mortality. Most patients with esophageal and gastric cardia cancer are often diagnosed at an advanced incurable stage with a poor overall survival. Dysphagia and obstruction in patients with advanced esophageal and gastric cardia cancer lead to inability to handle oral secretions, recurrent episodes of aspiration pneumonia, nutritional compromise, weight loss, weakness, debility and severe chest pain, compromising the quality of life. Patients with locally unresectable tumor and metastatic disease are treated with palliative intent. In this article we are going to describe the use of self expandable stent (SES) as non surgical, minimally invasive treatment options in symptomatic patients with advanced esophageal and gastric cardia cancer, who are not candidates for surgery, chemo-radiation or who have recurrent dysphagia following definitive treatment.*

Introduction

Esophageal carcinoma is the sixth most common cause of cancer mortality. The most common esophageal cancer in developed countries including the U.S. is adenocarcinoma. China, Iran and parts of Africa have a high incidence of esophageal squamous-cell carcinoma. Most patients with esophageal and gastric cardia cancer are often diagnosed at an advanced incurable stage with a poor overall survival of less than 9 months and five-year survival rate of less than 20%.^{1,2}

Dysphagia and obstruction in patients with advanced esophageal and gastric cardia cancer lead to inability to handle oral secretions, nutritional compromise, weight loss, weakness, debility, recurrent episodes of aspiration pneumonia and severe chest pain, compromising the quality of life. Therefore, dysphagia and obstruction are considered two of the most distressing and debilitating symptoms in patients with advanced esophageal cancer (*Figure 1, www.dcmsonline.org*). Patients with locally unresectable tumor and metastatic disease are treated with palliative intent.³

The most important aspect in palliation is directed toward relieving dysphagia and obstruction, restoring oral diet to maintain nutrition and providing an acceptable quality of life.⁴ The use of self expandable stent (SES) under these circumstances may allow for the avoidance of more invasive procedures such as the placement of gastrostomy and jejunostomy tubes. There are a wide variety of palliative treatments considered to relieve dysphagia and obstruction, including

chemotherapy (which has a limited role due to drug toxicity), external beam radiation therapy or local delivery radiotherapy also called brachytherapy (which do not provide immediate relief of the obstruction), or different endoscopic treatments including, injection ablative therapies (ethanol, cisplatin/epinephrine), laser therapy, argon plasma coagulation and photodynamic therapy.⁵⁻¹⁰

Self-expandable metal stent (SEMS) and self-expandable plastic stent (SEPS) have evolved since the early 1990s as a nonsurgical, minimally invasive treatment option in symptomatic patients who are not candidates for surgery, chemotherapy or who have recurrent dysphagia following definitive treatment. At the present time, placement of a SES is the most frequently used method for palliation for esophageal and gastric cardia cancer patients to relieve dysphagia and also has been indicated to occlude malignant esophago-respiratory fistula (ERF). Other indications for stent are phrenic or recurrent laryngeal nerve palsy.¹¹

These patients may benefit from endoluminal implantation of SES, which dramatically relieves dysphagia and obstruction, therefore, improving patient quality of life with a restoration of natural alimentation.^{1,2,12} SES can be carried out with a high technical success rate as a 20 minute outpatient procedure. SES has a low rate of stent placement complications and is considered an established part of palliative treatment; however, serious complication may occur. The complications can be classified as in early (< 7 days after procedure), which has been subdivided in intra-procedural complications, post procedure complications, and late complications (> 7 days after procedure). These complications include cardio-respiratory, hemorrhages; perforation, stent misplaced, stent migration, atypical chest pain, trachea-bronchial stenosis, fever, hemorrhage, perforation, aspiration pneumonia, esophageal reflux, recurrent food impaction, fistula formation, and tumor growth.¹³

Types of Stents

A variety of SES is available for the management of obstruction and ERF in patients with advanced esophageal and gastric cardia cancer. SES differs in design and physical properties and will depend upon the individual manufacturer. Many of the available SEMS are covered to reduce the risk of tumor in-growth and seal ERF.¹⁴ In cases where the distal margin of the stent crosses the gastro-esophageal (GE) junction; there are now SEMS available with an anti-reflux mechanism.¹⁵ SEPS has the characteristics of being removable, save during neoadjuvant treatment, and would not interfere with EUS staging, re-staging and follow-up imaging such as CT scan, PET scan or MRI.¹⁶ Self expandable esophageal stent loaded with iodine 125 (I 125) has been described.¹⁷ Recently

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introduced, a biodegradable stent made of poly-l-lactic acid monofilaments, which dissolve in a few months (3-4 mo), may be a good alternative in the near future.¹⁸ (Table 1).

Table 1 Self Expandable Stent Types

- Alimaxx-E stent (Alveolus, Charlotte, NC)
- Biodegradable stent (Ella-CS, Hradec Kradec Kralove, Czech Republic)
- Dual stent – anti reflux valve (Wilson Cook Medical, Winston – Salem, NC)
- Esophacoil (Medtronic/Instent Eden Prairie, Minnesota)
- Flamingo Wallstent II (Microvasive Boston Scientific Inc, Natick, MA)
- Gianturco Z-stent (Wilson Cook Medical, Winston – Salem, NC)
- Niti-S double stent (Taewoong Medical, Seoul, Korea)
- Polyflex stent (Boston Scientific, Natick, MA)
- Ultra-flex stent (Microvasive Boston Scientific Inc, Natick, MA)
- Wall Flex stent (Boston Scientific, Natick, MA)

No single study compares all the above models for cost, physical properties, technical success, complications, and assessment of long term benefits. However, studies suggest that stents are similar regarding dysphagia relief.

Verschuur et al randomized placement of an Ultraflex stent, Polyflex stent or Niti-S stent in 125 patients with dysphagia from inoperable carcinoma of the esophagus or gastric cardia. They conclude all three stents are safe and offer adequate palliation of dysphagia from esophageal or gastric cardia cancer. However, Polyflex stents seems the least preferable as placement of this device is technically demanding and associated with high rate of stent migration.¹⁹

Conio et al in a randomized prospective study of 101 patients with unresectable esophageal cancer found no difference in palliation compared with partially covered Ultraflex (metal) stent and Polyflex (plastic) stent. However, there were significantly more complications with the Polyflex stents.²⁰

Sabharwal et al in a prospective randomized study using Flamingo covered Wallstent or an Ultraflex covered stent in 53 patients with esophageal cancer localized in the lower third of the esophagus. In this study the two types of stents are equally effective in the palliation of dysphagia and the complication rates associated with their use are comparable.²¹

Technique

Once the decision is made to place a stent, several questions must be answered by the endoscopist. They are: Which is best - General anesthesia or conscious sedation? At what esophageal level is the lesion localized? What type of stent should be used? Should the stent be covered or uncovered? Should the lesion be pre-dilated or not? And in patients with esophageal - respiratory fistula, which stent should be placed first, esophageal or respiratory (tracheal or bronchial) stent?

The majority of esophageal SES can be performed under conscious sedation. This author prefers general anesthesia. No single study compares all the stent models and at present time there is no demonstrable superiority of one design. It depends on personal experience and preference. The patient is usually placed in the left lateral position. Tumor dilation is necessary in some cases. Dilation up to 10-12 mm is recommended

prior to deployment of the stent for some manufacturers (Polyflex stent). For stricture dilation, Balloon, wire guided Bougie or a Savary-Guillard dilator over a guide wire can be used (Figure 2, www.dcmsonline.org). Dilation of the stricture is carried out under endoscopic, fluoroscopy guidance, or both (author prefers dual guidance). Dilation of the stricture is done under endoscopic, fluoroscopic and both guidance. Once the tumor is dilated, the length of the stenosis must be accurately measured. This can be accomplished endoscopically and/or fluoroscopically by visualization and documentation of distance measured from incisors, to the upper and lower margin of the tumor. Usually these margins are then marked using externally placed “paper clips” or internally placed hemoclips (used for hemostasis) prior the stent deployment. Once the SES is in a good position (stent covered at least 3-4 cm longer than upper and lower tumor margins), it is deployed under endoscopy, fluoroscopy or both guidance. The level of technical support from industry and the availability of expert physicians are important factors that contribute to successful stent placement²²(Figures 3-4, www.dcmsonline.org).

All patients with a stent crossing the gastro-esophageal junction are informed of the likelihood of severe reflux for which Proton pump inhibitors (PPIs) may be prescribed. (Figure 5, www.dcmsonline.org) For patients with ERF and those with a tumor in the proximity of the airway (trachea or bronchi), it is recommended that a respiratory covered stent be placed first to avoid compression of the airway by esophageal stent and the patient be placed on indefinite suppressive antibiotics in an attempt to reduce morbidity from pneumonia.²³⁻²⁶ Patients are observed for a few hours before discharge. Difficult cases are admitted for overnight observation. Radiology confirmation of the stent position, reopening of the esophagus stricture and ERF closure is recommended (Figure 6, www.dcmsonline.org). The patient is advised to consume liquids and soft mechanical diet to avoid food impaction.

Indications of Self Expanding Stent

Stent is probably one of the best options and is recommended in patients with dysphagia caused by esophageal or gastric cardia cancer and a life expectancy of 3 month or less.²⁷ SES is generally seen as a palliative treatment since it has no ablative effect on the tumor. Many sitting stents are used only when other treatments have failed for patients with poor prognosis.

Indications for self expanding stent have two categories: absolute and relative as opposed to surgical resection. Absolute indications are: Advance esophageal cancer with distant metastasis; Tracheo - esophageal Fistula (in conjunction with respiratory stent); Phrenic or recurrent laryngeal nerve palsy; and Patient not being candidate for radiotherapy/chemotherapy or other form of treatment. Relative indications are: Older age (80 or older); Extreme cachexia/malnutrition; Multiple medical co-morbidities and Esophageal stent as a bridge to surgery (and its potential effect on the nutritional status prior to surgery, need to be studied).

Contraindications of Self Expanding Stent

Self expanding stent has absolute and relative contraindications. Absolute contraindications are: Tumor involving the upper esophageal sphincter. Relative contraindications are: Extensive cancer involving gastric cardia and While patient is undergoing induction therapy (chemo-radiation).

Complications

Self expanding stents (SEMS and SEPS) are very attractive options in the management of patients with end-stage esophageal and gastric cardia cancer. Relief of the dysphagia is immediate (>90% of the cases). However, stent placement is not always easy to perform and is not free of complications. Traditionally, complications have been classified as early and late complications. Other authors classify them as an intra-procedural, post procedural or delayed complications. Overall 41.6% of patients had at least one complication after stent placement. The mortality is < 5% at 1 week and <30% at 30 days.²⁸

Complications are also related to the site of the stent placement. For proximal stents the foreign body sensation and respiratory symptoms are the most common reported symptoms. For distal stents, mainly those placed through the GE-junction, intractable reflux requiring the use of proton pump inhibitors (PPIs) is the most common reported symptom.

Additionally, each of the stents has its own complications; for instance self expanding plastic stent (SEPS) or Polyflex stent has been associated with high rates of migration, the lesion must be pre-dilated (10 to 12 FR) due to large delivery system, thus perforation is high in fibrotic and poorly distended lesions, mainly those who have been previously treated with chemo/radiotherapy.²⁹ There have been various types of SEMS with their own shortcomings. For instance, covered metallic stent has been shown to migrate more frequently than uncovered stent.³⁰ Uncovered stents have been associated with increased rate of tumor ingrowths compared with covered metal stent. However the use of Photodynamic Therapy (PDT) to treat tumor in growth through self expanding metal esophageal stents has been described as effective and safe.^{8,31} Recurrent dysphagia occurs in almost one-third of patients after stent placement. Repeat interventions for stent-related recurrent dysphagia are effective in over 90% of patients.³² Prior irradiation and/or chemotherapy increase the risk of persistent chest pain after stent placement.³³ There are early and post procedural complications. They are: **Early complications (<7 days):** A-1 Intra-procedural complications: Associated with sedation per se such as cardio-respiratory complications, iatrogenic perforation, hemorrhages or stent malposition or inadequate deployment (above superior esophageal sphincter, with a consequent foreign body sensation) and A-2 Post procedural complications: Hemorrhages, perforation, severe chest pain (atypical chest pain), respiratory compromise due to airway compression with resulting asphyxia. **Late or delayed complications (> 7 days):** Hemorrhages, perforation, severe recalcitrant esophageal reflux, stent migration, ulcerations, trachea-esophageal fistula, in-growth or overgrowth tumor and occlusion of the stent (food impaction).

Prognosis

Survival of patients with esophageal cancer is often poor; five year survival is less than 20%.^{1,2} Although SES has no direct anti-tumor activity, stenting the esophagus has dramatically improved the quality of life of patients with end-stage esophageal cancer.^{4,34} This application probably extends the survival of symptomatic, inoperable patients by preventing aspiration pneumonia, dehydration and improving nutritional intake. The median survival after SES placement

ranges from 49 to 186 days^{25,35,36,37} However, it is important to note that if anorexia is secondary to the presence of the tumor and not due to its mechanical implications, stenting is not likely to have a major impact on nutrition. Anorexic patients will benefit from a feeding tube with a fixed amount of caloric intake.

Summary and Recommendations

SEMS and SEPS are nonsurgical, minimally invasive treatment options in symptomatic patients with advanced esophageal and gastric cardia cancer, who are not candidates for surgery, chemo-radiation or who have recurrent dysphagia following definitive treatment. Stents may also benefit patients with Esophageal-respiratory fistula (ERF) and phrenic or recurrent laryngeal nerve palsy. SEPS placement is safe, dysphagia score improve in a statistically significant manner. However, stent migration is a common event. Seeps are removable, safe during neoadjuvant treatment, and would not interfere with EUS staging and follow-up imaging such as CT scan, PET scan or MRI.

Esophageal stents related complications can be early (< 7 days after procedure) or late complications. These complications include cardio-respiratory, hemorrhages; perforation, stent misplaced, stent migration, atypical chest pain, trachea-bronchial stenosis, fever, hemorrhage, perforation, aspiration pneumonia, esophageal reflux, recurrent food impaction, fistula formation, and tumor in-growth or overgrowth tumor. Stents crossing the gastro-esophageal junction can cause severe reflux and PPI maybe prescribed.

For tumor or strictures in the upper third of the esophagus, the proximal end of the stent should be within or below the upper esophageal sphincter. Patients with ERF and those with tumor in the proximity of the airway (trachea or bronchi), should receive a respiratory covered stents first to avoid compression of the airway by the esophageal stents. Suppressive antibiotics are recommended to reduce morbidity from pneumonia. Self expandable esophageal stent loaded with iodine 125 (I 125) and the recently introduced biodegradable stent made of poly-l-lactic acid monofilaments, which dissolve in a few months can be a good alternative in the near future.

Although SES has no direct anti-tumor activity, stenting the esophagus has dramatically improved the quality of life of patients with end-stage esophageal cancer.^{4,35} The median survival after SES placement ranges from 49 to 186 days.

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Figure 1. Advanced Esophageal Cancer



Figure 2. Stricture Dilation

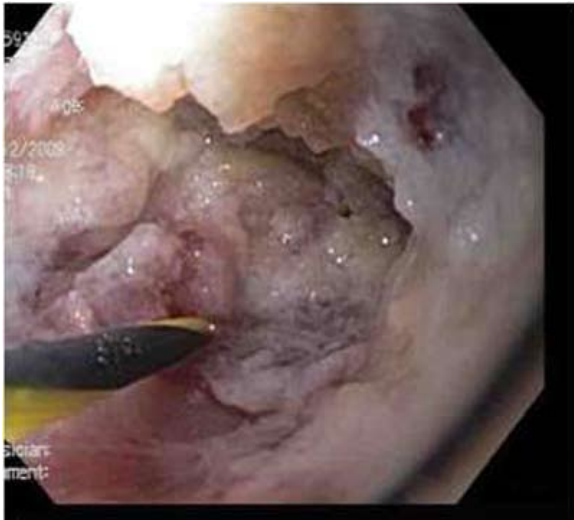


Figure 3. Stent Placement



Figure 5. Proton Pump Inhibitors



Figure 6. Radiology Confirmation of the Stent Position

