

## Stent placement in esophageal cancer as a bridge to surgery

Approximately 40% to 50% of patients with esophageal cancer have operable disease at presentation, and the majority of them present with malignant dysphagia. However, before surgical resection takes place, many weeks pass, filled only with neoadjuvant therapy or (unfortunately) mere waiting on the surgical waiting list. During this period, patients continue to be unable to eat normally and often need some form of enteral feeding, such as nasogastric tube or PEG feeding. These treatment options, however, have the major disadvantage that they do not relieve dysphagia, the patients' main symptom. Furthermore, long-term nasogastric feeding tubes may cause nasal irritation and/or sinusitis. Placement of a PEG is not without risks and may lead to worsening of the operative outcome because this device may compromise the stomach, which is often used as a conduit to replace the esophagus during esophagectomy. Moreover, stomal seeding of cancer or skin and soft-tissue infections may also adversely affect the patients' prognosis. So why not place a temporary esophageal stent as a "bridge to surgery" because this may improve malignant dysphagia as well as the patients' nutritional status?

In this issue of *Gastrointestinal Endoscopy*, Adler et al<sup>1</sup> report their outcomes in 13 prospectively evaluated patients with locally advanced esophageal cancer treated with a self-expanding plastic stent (SEPS) to relieve malignant dysphagia during neoadjuvant therapy. The stents were placed immediately after staging with EUS. Although this result was not unexpected, dysphagia scores improved significantly after placement of a Polyflex stent (Boston Scientific, Natick, Mass). No major complications, such as esophageal perforation and bleeding, were observed, and all patients, except one who had severe retrosternal pain, were discharged home the same day.

The physicians who performed this study must be very enthusiastic about these results because they decided to incorporate SEPS placement into their routine clinical care after the study ended. Should we all follow their example, or do we need additional information before we can make a proper decision?

As of this writing, data on only 23 patients treated with a temporary preoperative esophageal stent have been published.<sup>1-3</sup> Amelioration of dysphagia was found in nearly all

these patients. Improvement of malignant dysphagia, however, although very important, is not the only clinical parameter that matters in these patients. The ultimate goal of treating patients with resectable esophageal cancer should be improvement of long-term survival rates. Therefore, it should be clear that surgical resection and neoadjuvant therapy are not hampered by endoscopic placement and possible removal of a temporary self-expandable esophageal stent. These safety data are not (yet) available. In the study by Adler et al,<sup>1</sup> only 3 of 13 patients underwent an esophagectomy, and none of them had a stent that was still in the correct position. In 2 previously published retrospective smaller series of patients, no surgical problems were

**It should be clear that surgical resection and neoadjuvant therapy are not hampered by endoscopic placement and possible removal of a temporary self-expandable esophageal stent, but such safety data are not (yet) available.**

mentioned either, although the amount of information provided in these studies was very limited.<sup>2,3</sup>

A randomized study aimed at showing no difference in survival rates in resectable patients with or without a bridge to surgery stent will probably not be performed in the future. However, other robust study endpoints, such as the pathological TNM stage of the tumor, an R0 resection, or surgical complications, eg, anastomotic leakage, could be used in a randomized trial to assess safety of pre-esophagectomy stent placement. In my opinion, demonstration of similarity in these clinically relevant parameters is crucial before we can decide whether this is a safe procedure.

What are the potential risks of esophageal cancer stent placement as a bridge to surgery? In the study by Adler et al,<sup>1</sup> no major complications occurred during neoadjuvant chemoradiotherapy with an expandable plastic stent in situ. Esophageal perforation is probably the most serious adverse event of stent placement because subsequent tumor spill in the pleural cavity will decrease the chance of a curative resection. Esophageal perforation rates varying from 0% to 5% have been found in patients treated with an SEPS in a palliative setting.<sup>4-6</sup> Data on perforations after neoadjuvant therapy in patients with an SEPS in situ are

scarce.<sup>7,8</sup> Yakami et al<sup>7</sup> described 3 patients who received a self-expanding esophageal stent before radiotherapy for unresectable or metastasized cancer. One of these 3 patients received an SEPS and died of perforation 2 months after undergoing radiotherapy.

The Polyflex stent, a totally covered, thin-walled, self-expanding silicone device with an encapsulated monofilament polyester braid, has some features that might increase the risk of esophageal perforation.<sup>6</sup> The applicator in which the stent is loaded before placement has a diameter of 12 to 14 mm depending on stent size and is rather rigid. In addition, the dilator at the tip of the introducer system is short, which may complicate its passage across angulated strictures due to inappropriate transmission of force. A second drawback of the Polyflex stent is its known relatively high migration rate, particularly in cases with distal stenosis in which this is a significant problem. Migration rates range from 13% to 29% in randomized studies comparing SEPSs with self-expanding metal stents (SEMSs) in patients with unresectable esophageal cancer.<sup>5,6</sup> In the current study by Adler et al,<sup>1</sup> 6 of 13 stents (46%) migrated at some point. As the authors already mentioned, some of the migrations were likely a sign of response to neoadjuvant therapy. Moreover, 12 of 13 patients had a tumor in the lower part of the esophagus. Stents were not automatically replaced when migration occurred because the lumen was thought to be adequate for a liquid diet. In my opinion, this does not correspond well to the main aim of the study, which was to relieve malignant dysphagia. A liquid diet is often also realizable without any intervention at all.

A different type of stent may therefore be more suitable for this indication. SEMSs have a lower migration rate and are more flexible than SEPSs. Partially covered SEMSs, such as the Ultraflex stent (Boston Scientific) and the Evolution stent (Cook, Limerick, Ireland), have a layer that covers only the midsection of the stent. At the uncovered proximal and distal ends of these stents, hyperplastic tissue grows into the mesh, which makes endoscopic removal of a partially covered stent after a period of approximately 1 month difficult and hazardous. If removability of the stent is necessary, which may be the case in temporary stent placement, a partially covered stent is not an attractive option. Conversely, the stent could also be left in place because it will be removed during esophagectomy. A fully covered SEMS has the disadvantage of embedding in the esophageal wall to a much lesser degree and can be removed much more easily. This type of metal stent could therefore be an alternative for the Polyflex stent. The argument of Adler et al not to use metal stents was that possible restaging evaluations would then have been complicated because of the interference of metal in imaging studies. The recently introduced biodegradable stent (Ella-CS, Hradec Kralove, Czech Republic) made of poly-L-lactic acid monofilaments, which dissolve in a few months, could therefore be a good alternative in this patient category in the near future. Many data on safety and migration rates of this type of stent, however, are not yet available.

Another important aspect of stent placement in esophageal cancer as a bridge to surgery that needs to be studied is its potential effect on the nutritional status. Undernutrition has been reported to occur in 79% of patients with esophageal cancer before starting treatment.<sup>9</sup> This is most likely not only caused by local tumor obstruction but also by anorexia and cancer cachexia. Baseline nutritional status has been shown to be an independent predictive factor of complete response to chemoradiotherapy and survival in patients with nonmetastatic esophageal cancer treated with curative intent by definitive chemoradiotherapy.<sup>10</sup> It is unclear whether stent placement will lead to significant improvement of nutritional status.<sup>11</sup> If anorexia secondary to the presence of a GI carcinoma is causing weight loss, stent treatment will likely not have a major impact on nutrition. In that case, nasogastric tube or PEG feeding with a fixed amount of calories may be more beneficial for the patients' nutritional status. In contrast, cancer cachexia, which is characterized by involuntary weight loss and muscle wasting due to circulating cytokines and tumor peptides, will not respond to a forced increase in caloric intake.<sup>12</sup> Therefore, changes in body weight, body mass index, or serum albumin level should be measured in a trial comparing a temporary esophageal stent with enteral feeding. A proper quality-of-life and pain assessment, instead of dysphagia scores alone, is also necessary because stenting of the esophagus may induce pain, which is fortunately most often of short duration. Besides safety, quality of life, and impact on nutritional status, another aspect of stent placement in esophageal cancer as a bridge to surgery that needs further evaluation is cost. The initial cost of stent placement will be higher than that of nasogastric tube or PEG placement because of the high cost of stents. It remains to be seen how this translates into a cost-effectiveness analysis of the entire treatment period.

The limitations of the study by Adler et al<sup>1</sup> notwithstanding, it has provided interesting data on a new indication for esophageal stents. Nevertheless, at present, I would not advise following the investigators' policy of placing a stent in all patients undergoing neoadjuvant therapy for resectable esophageal cancer. The use of a stent as a bridge to surgery should be limited to well-designed clinical trials.

## DISCLOSURE

*The author disclosed no financial relationships relevant to this publication.*

**Frank P. Vleggaar, MD, PhD**

*Department of Gastroenterology and Hepatology  
University Medical Center Utrecht  
Utrecht, The Netherlands*

*Abbreviations: SEMS, self-expanding metal stent; SEPS, self-expanding plastic stent.*

## REFERENCES

1. Adler DG, Fang J, Wong R, et al. Placement of Polyflex stents in patients with locally advanced esophageal cancer is safe and improves dysphagia during neoadjuvant therapy. *Gastrointest Endosc* 2009;70:614-9.
2. Siddiqui AA, Loren D, Dudnick R, et al. Expandable polyester silicon-covered stent for malignant esophageal strictures before neoadjuvant chemoradiation: a pilot study. *Dig Dis Sci* 2007;52:823-9.
3. Martin R, Duvall R, Ellis S, et al. The use of self-expanding silicone stents in esophageal cancer care: optimal pre-, peri-, and postoperative care. *Surg Endosc* 2009;23:615-21.
4. Szegedi L, Gal I, Kosa I, et al. Palliative treatment of esophageal carcinoma with self-expanding plastic stents: a report on 69 cases. *Eur J Gastroenterol Hepatol* 2006;18:1197-201.
5. Conio M, Repici A, Battaglia G, et al. A randomized prospective comparison of self-expandable plastic stents and partially covered self-expandable metal stents in the palliation of malignant esophageal dysphagia. *Am J Gastroenterol* 2007;102:2667-77.
6. Verschuur EM, Repici A, Kuipers EJ, et al. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia cancer: a randomized trial. *Am J Gastroenterol* 2008;103:304-12.
7. Yakami M, Mitsumori M, Sai H, et al. Development of severe complications caused by stent placement followed by definitive radiation therapy for T4 esophageal cancer. *Int J Clin Oncol* 2003;8:395-8.
8. Nishimura Y, Nagata K, Katano S, et al. Severe complications in advanced esophageal cancer treated with radiotherapy after intubation of esophageal stents: a questionnaire survey of the Japanese Society for Esophageal Diseases. *Int J Radiat Oncol Biol Phys* 2003;56:1327-32.
9. Riccardi D, Allen K. Nutritional management of patients with esophageal and esophagogastric junction cancer. *Cancer Control* 1999;6:64-72.
10. Di Fiore F, Lecleire S, Pop D, et al. Baseline nutritional status is predictive of response to treatment and survival in patients treated by definitive chemoradiotherapy for a locally advanced esophageal cancer. *Am J Gastroenterol* 2007;102:2557-63.
11. Lecleire S, Di Fiore F, Antonietti M, et al. Undernutrition is predictive of early mortality after palliative self-expanding metal stent insertion in patients with inoperable or recurrent esophageal cancer. *Gastrointest Endosc* 2006;64:479-84.
12. Ockenga J, Valentini L. Review article: anorexia and cachexia in gastrointestinal cancer. *Aliment Pharmacol Ther* 2005;22:583-94.

**Availability of Journal back issues**

As a service to our subscribers, copies of back issues of *Gastrointestinal Endoscopy* for the preceding 5 years are maintained and are available for purchase from Elsevier until inventory is depleted. Please write to Elsevier Inc., Subscription Customer Service, 6277 Sea Harbor Dr., Orlando, FL 32887 or call 800-654-2452 or 407-345-4000 for information on availability of particular issues and prices.