

Stents for the long haul: what do we need?

Over the past 15 years, self-expanding metal stents (SEMSs) have become the standard for palliation of inoperable malignant dysphagia, replacing their rigid plastic predecessors. Initially composed of bare steel wire mesh, stents were designed in a dog-bone configuration to embed in tumor and resist migration. Modern stents are now made of nitinol, a flexible nickel-titanium alloy, compressed on slim-line delivery catheters, essentially eliminating the need for preplacement dilation. Stents have also evolved a partial covering with a polyurethane or silicone membrane to resist tumor ingrowth through the wire mesh, and the proximal end is flanged to reduce migration. The partial covering allows the exposed bare mesh at the ends of the stent to, it is hoped, embed in the mucosa to provide anchoring. Tumor ingrowth and overgrowth can still occur through the exposed proximal and distal mesh, but can be minimized by choosing a stent long enough to allow generous overlap of the tumor by the covered stent segment. Thus, overall, tumor ingrowth rates with partially covered SEMSs have decreased, but at the expense of an increased stent migration rate (compared with uncovered SEMSs). With adenocarcinoma being the dominant esophageal cancer histology in the Western world and predominantly located in the distal esophagus, migration is a significant issue. Given the need to bridge the esophagogastric (EG) junction in most esophageal/gastric cardia adenocarcinomas, only the proximal bare wire flange can embed in the mucosa and anchor, while the distal end dangles within the gastric lumen. The main goal of stenting in inoperable esophageal cancer is palliation of dysphagia with resultant improved quality of life because of continued oral intake. Improved quality of life is also reflected in the short- and long-term complication rates of stents, notably maintenance of prolonged luminal patency, which prevents return trips to the GI laboratory for the terminal patient. Unfortunately, the perfect stent does not yet exist despite a flurry of industry competition to create one that is simple to deploy, stays where it is placed, and is resistant to tumor/tissue ingrowth and overgrowth.

Nontumoral occlusion caused by hyperplastic tissue response at the ends of partially covered SEMSs also remains a current drawback, requiring reestablishment of luminal

patency via ablative techniques or coaxial stent placement. Aiming at decreasing such a hyperplastic response, a self-expanding plastic stent with a more “tissue-friendly” design was introduced (Polyflex; Boston Scientific, Natick, Mass). Made of a polyester skeleton with a full silicone coating, this endoscopically removable device was marketed for malignant and benign refractory strictures and occlusion of tracheoesophageal fistulae. Given the fully covered plastic design, the hyperplastic tissue response is less at the flanged ends; however, its delivery system is large and cumbersome, and the migration rate is significant, which deters

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many from using this stent in malignant strictures. Therefore, fully covered SEMSs have evolved that should theoretically resist tumor ingrowth, reduce hyperplastic tissue overgrowth, stay in place, and allow removal.

The Alimaxx-E stent (Alveolus, Charlotte, NC), first introduced in 2005, is marketed as a hybrid stent, offering the advantages of both metallic and silicone stents. It is approved for maintaining luminal patency in esophageal strictures caused by intrinsic or extrinsic malignancy and for occlusion of esophageal fistulae. Made of nitinol, it is fully covered with polyurethane and has 20 outer metal struts to resist migration. Given the fully covered design with a proximal suture to grasp for repositioning, this stent is also theoretically removable. In this issue of the journal, Uitdehaag et al¹ describe their experience with this stent for the palliation of malignant dysphagia in 45 patients. This very experienced group of investigators randomized the use of 2 different deployment systems for Alimaxx-E stent placement: introduction over a guidewire (Alimaxx-E GW) versus direct visualization via a new delivery catheter loaded over a small-caliber endoscope (Alimaxx-E DV). Two different stent sizes were also used (18-mm vs 22-mm internal diameter). However, the choice of size was not random; the larger stent was chosen if “pre-stenotic dilation was observed during endoscopy.” Difficulty was encountered traversing the stricture with the DV system in almost half (11/23) of the patients, likely because of the larger

deployment system (30F). In total, 38% of patients experienced major or minor complications, not significantly different compared with data reported in the existing literature. However, all 5 early (< 1 week) major complications (severe pain, hemorrhage, fever) occurred with use of the DV system.

The dysphagia score improved significantly in all patients at 4 weeks after stent placement; however, recurrent dysphagia developed in 49% (22/45) of patients during follow-up. The overall stent migration rate was high at 36% (16/45), with an additional 7 and 4 patients experiencing tissue overgrowth and food impaction, respectively. In univariate analysis, the only variable associated with migration was tumor histology (adenocarcinoma). This is likely reflected in the facts that adenocarcinomas are predominantly located in the distal esophagus/gastric cardia, necessitating stent placement across the EG junction, and that the stent is fully covered. Indeed, of the 16 stents that migrated in this study, 13 were placed in the setting of esophageal or gastric cardia adenocarcinoma. The adenocarcinoma cohort consisted of 29 patients; thus, the migration rate was 45% for stents used for palliation of obstructing adenocarcinoma. Because adenocarcinoma is the dominant histology, this migration rate is simply too high. Furthermore, the majority of stents that migrated in this study were large-diameter stents (10/16) because they were predominantly placed across the EG junction. Uitdehaag et al¹ subjectively comment that an adapted design with 45 antimigration struts (compared with 20) decreases the migration rate; we will need to see the objective data.

The messages that I take away from the Uitdehaag et al study evaluating the Alimaxx-E stent are twofold. First, avoid the DV deployment system. There is no appreciable advantage, and the complication rate is higher. If fluoroscopy is not available, use the GW system under direct endoscopic visualization or choose another stent. Second, exercise caution before placing this stent to palliate adenocarcinoma of the distal esophagus/gastric cardia (ie, across the EG junction). The chance of it migrating is essentially a coin toss.

Retrieving migrated stents can at times be problematic with heightened risk. Fortunately, in this study, the migrated stents were safely retrieved, except one for which surgery was required for its removal because it had migrated into the small bowel. However, this particular stent may be prone to fracture while attempting removal or retrieval. There are 6 reports in the MAUDE (Manufacturer and User Facility Device Experience) database reporting stent fracture, with an additional 2 case reports in the literature.^{2,3} Several instances resulted in major complications necessitating intubation, intensive care unit-level care, and extended hospital stay.

Eloubeidi and Lopes⁴ recently reported their experience using the Alimaxx-E stent in a variety of settings (malignant dysphagia, refractory benign strictures, tracheoesophageal fistula, perforation). They removed 22 of 36 stents uneventfully; although 1 fractured, it was still removed without inci-

dent. There was a 36% migration rate, and, overall, 31% of patients had recurrent dysphagia. Stents that traversed the EG junction were 7.5 times more likely to migrate. Given the mixed patient population in their report, it is difficult to make direct comparisons with the Uitdehaag et al study.

Although there is no gold-standard esophageal stent, the Ultraflex partially covered stent (Boston Scientific) seems to be the most commonly placed stent throughout the world.¹ Even so, there may be recurrent dysphagia as much as 52% of the time because of stent migration, tumor/tissue overgrowth, and/or food bolus impaction,⁵⁻⁸ but this rate is significantly reduced with use of a larger-diameter stent.⁷ As previously mentioned, intense industry competition abounds in the hopes of claiming a "piece of the action." Each new stent model is touted as better than its predecessor and competitor. Delivery systems are slim line and user friendly, and stents are reported to have stronger radial force. The WallFlex stent (Boston Scientific) and the Evolution stent (Wilson-Cook Medical, Winston-Salem, NC) are 2 recently introduced stents. However, there is no clinical evidence or research proving superiority over any existing stent.

Two fully covered SEMSs, manufactured by Korean companies, have been available in Europe. Each comes in multiple designs for anatomic variations and has a full silicone cover, a retrieval lasso, and a dog-bone configuration. The Bonastent (Standard Sci-Tech, Seoul, Korea), not available in the United States, also has one design with an S-shaped antireflux valve. The Niti-S stent (Taewoong-Medical, Seoul, Korea) boasts 26-mm dog-bone flanges to deter migration. There is one design (Head-type) that is now approved by the U.S. Food and Drug Administration and available in the United States, with indications for both malignant and benign disease; thus, it is removable. The double-type stent, a version of which offers an antireflux valve, is specifically designed to resist migration in malignant strictures. Essentially a stent within a stent, this double-layered design consists of a fully covered inner stent with an outer uncovered nitinol sleeve. Thus, it resists tumor ingrowth while having the antimigration properties of an uncovered stent.

Based on currently available data, much of which has been published by the Dutch group, the double-type Niti-S stent appears to have the lowest migration rate in the literature. Pooled data from 3 studies reveal an overall lower rate of recurrent dysphagia for the Niti-S double-type stent (19%), with a migration rate of 8% (8/101).⁸⁻¹⁰ This is a favorable profile compared with that of the Ultraflex stent. The only advantage of the Polyflex stent seems to be the lower rate of tissue overgrowth because the polyester backbone seems to be less traumatic to esophageal mucosa than nitinol.⁸

Overall, currently available esophageal stents seem to improve malignant dysphagia to a similar degree and have comparable complication rates. Aside from safe placement, our main goal in these terminal patients is to palliate dysphagia and improve quality of life. To this end, prevention

of recurrent dysphagia is an important issue and the main problem with which endoscopists continue to struggle. Gastroenterologists vested in this practice must be cognizant of stent design nuances and be knowledgeable of existing data. Because no perfect stent currently exists, the one with which the endoscopist is most familiar usually wins out. Given the unacceptably high migration rate of the Alimaxx-E stent in the setting of adenocarcinoma, caution must be exercised before choosing this device. The Dutch group has clearly led the way in stent evaluation. Given their track record, we will continue to look to them for the defining comparative randomized trials in this arena.

So what do we need for the long haul? We need a user-friendly stent design that resists migration and tissue overgrowth for the long-term palliation of malignant dysphagia. Perhaps a true hybrid stent is necessary, a “SEMPS” (self-expanding metal and plastic stent), if you will—most likely a nitinol stent composed of a covered middle section wrapped in bare mesh with tissue-friendly proximal and distal flanged ends coated with plastic to avoid metal wire contact with the mucosa. This will be a challenge for the engineers of industry.

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Kevin McGrath, MD
*Division of Gastroenterology
 Hepatology, and Nutrition*

*University of Pittsburgh Medical Center
 Pittsburgh, Pennsylvania, USA*

Abbreviations: EG, esophagogastric; SEMS, self-expanding metal stent.

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