Fully Covered Esophageal Stents: Role in Benign Disease

Self-expanding metal esophageal stents have been first line of therapy in the palliation of malignant esophageal strictures for many years. The stents most commonly used in palliation are partially covered, and thus are essentially non-removable. The fully covered stents, with their potential for removability, have revived interest into using minimally invasive techniques to treat benign esophageal conditions including benign esophageal diseases such as strictures, perforations, leaks and fistulas that would otherwise require surgery. This review discusses the types of fully covered esophageal stents and the data behind their use in a variety of benign esophageal conditions.

INTRODUCTION

The use of self-expanding metal esophageal stents for the palliation of malignant esophageal strictures has been widely accepted. Since the stents used in palliation are partially covered, they are essentially not removable. Partially covered nitinol metal stents have a plastic membrane along the body of the stent with uncovered segments at both ends. The plastic membrane lining prevents tumor in-growth into their lumen. With this design, the uncovered exposed ends of the stent become embedded into the tissue, which prevents migration of the stent, but at the same time, makes it nearly impossible to remove. Due to the difficulty associated with removing these stents, they have not gained popularity in the treatment of benign esophageal diseases and their use in the management of benign disease is unclear. Prolonged stent embedment in benign esophageal tissue can result in significant complications such as ulceration, bleeding, fistula, dysphagia and new stricture formation if the stent is not removed. One study found that 80% of the patients that had partially covered stents placed for benign strictures had one of above-mentioned complications. Another study found stent induced stenosis secondary to granulation tissue ingrowth with extended use.

Fully covered esophageal stents address some of the burdens associated with the partially covered stents. A fully covered stent would, in theory, deter tissue granulation along the entire body of the stent and thus be easily removable. Baron et al. confirmed this theory through their study on pigs. They found that partially covered stents became embedded secondary to tissue granulation, which made removal of the stent traumatic in comparison to the fully covered stent which had limited tissue embedment and were thus easily removable. Eloubeidi et al. took this a step further as

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they applied this theory to humans and found that while tissue reaction to fully covered stents was common, it was clinically insignificant. This concept sparked a new wave of interest into fully covered stents and their use in benign esophageal diseases. This review will focus on the temporary placement of fully covered esophageal stents for the treatment of esophageal strictures, leaks, perforations and trachea-esophageal fistulas.

### Characteristics of Esophageal Strictures

The majority of benign esophageal strictures result from long standing, uncontrolled gastroesophageal reflux. These strictures are often categorized as simple or complex. “Simple strictures” are smooth, straight and short, which makes them easily accessible with an endoscope. The remaining 25% of benign strictures are “complex” and result from radiation, sclerotherapy, chemical ingestion, surgery or rare dermatological issues. Complex strictures are long, narrow and torturous, which makes treatment through standard endoscopic techniques (such as dilators) difficult. The goal of therapy for strictures is dysphagia resolution and prevention of stricture recurrence, which is often accomplished through dilation.

Prior to any endoscopic intervention, it is crucial to ensure that the stricture is benign. This involves a three-step process of endoscopy, biopsy and then dilation at different times. A small study evaluated the safety of performing these three procedures in one sitting. The study followed 48 patients who underwent esophageal dilation following biopsy and found no complications related to the biopsy. This method provides reassurance that the stricture is benign, while simultaneously, allowing early intervention and thus, sooner symptomatic relief.

Despite intensive and repeated dilation, up to 40% of benign strictures recur. Simple strictures tend to respond better to dilation and acid control, however, complex strictures do not and tend to recur within weeks of therapy. Strictures that tend to recur despite intensive intervention are termed refractory benign esophageal strictures (RBESs).

Several alternative endoscopic options have been used to treat these RBESs. These options include intralesional injection of corticosteroids, electrocautery incision (of shatzki rings) as well as removable esophageal stents. For the purpose of this review, we will focus on the role of fully covered, expandable esophageal stents. Dilation entails a few seconds of stretching the stricture, which can temporarily increase luminal diameter. With this in mind, it is logical to assume that an expandable esophageal stent, which will maintain lumen patency but also function as a dilator slowly stretching the stricture for weeks, should lead to long lasting dysphagia relief. While in theory this
Fully Covered Esophageal Stents

(continued from page 40)

makes sense, no major prospective, randomized studies comparing stents with dilation have been done. Despite this, many small, retrospective case series and reviews have been written.

Types of Fully Covered Esophageal Stents

There are two major types of fully covered esophageal stents: fully covered self-expanding metal stents (FC-SEMSs) and fully covered self-expanding plastic stents (SEPSs).

FC-SEMSs are made of a wire mesh composed of a variety of metal alloys, most commonly nitinol. The wire mesh can confine to a thin diameter, allowing for easy delivery through narrow strictures. Some, but not all, have a dog bone shape, which reduces the chance of stent migration. They come equipped with a suture at the upper end of the stent, allowing for stent repositioning and easy access for stent withdrawal. The stents come preloaded, which allows for better positioning and are thought to be more user-friendly than their plastic counterparts. FC-SEMSs come in a variety of lengths and diameters. Those commonly available FC-SEMS in the United States are shown in Table 1.

SEPSs are made of polyester mesh and are fully covered with an inner lining of silicone. Polyflex (Boston Scientific) is a SEPS that has been FDA approved for use in benign esophageal conditions. The Polyflex stent has potential advantages in comparison to the metal stents mentioned above in that plastic causes less tissue activation than metal; therefore, plastic stents induce less tissue granulation. However, the plastic stents are not preloaded in a catheter and cannot constrict as well as the metal stents. This makes deployment into narrow areas difficult. Often times, pre-insertion dilation is also required, which in theory can increase the risk of esophageal perforation.

All of the stents come in a variety of sizes. Determining which stent to use should be based on the severity/length of stricture, perforation or leak as well as the features of the stent.

Fully Covered Self Expanding Plastic Stents (SEPS)

Several small studies have shown that temporary placement of SEPSs can be effective in managing patients with RBESs.12-17 (Figure 1) Published data on the efficacy of the Polyflex stent for the therapy of benign strictures has been mixed; while small, clinical studies prove that symptomatic relief from RBESs is achieved, there remains concern regarding stent migration. The largest published study was done by Dua et al. where they treated 40 patients with a Polyflex stent for four weeks.12 They reported successful stent placement and removal in 95% and 94% of their patients, respectively. At one year follow up, 40% of their patients were dysphagia free. The main complication was a 22% stent migration rate. On the other hand, Repici and associates13 treated 15 patients with RBESs with a polyester stent for 6 weeks with only one stent migration. The remaining stents were removed easily. At a 22-month follow up, they found resolution of strictures in 80% of their patients. A study done by Oh17 further echoed the results of the other studies. They found that while the Polyflex provided satisfactory relief of dysphagia secondary to RBESs, stent migration was quite frequent (64%). A systemic review of ten different studies which included 130 patients with RBES, reported successful insertion of stent in 128 of 130 (98%) of patients. Of these 128 patients, 68% remained symptom free 13 months after stent removal. However, stent migration occurred in 23% of patients within four weeks.14 Overall, multiple published studies as well as a systemic review all conclude that symptomatic improvement of dysphagia is achieved with the Polyflex; however, stent migration remains a major concern.

Fully Covered Self Expanding Metal Stents

FC-SEMSs are not FDA approved for use in benign esophageal diseases, although this is commonly performed in clinical practice in an off-label manner. (Figure 2) There are small studies pertaining to their use of FC-SEMSs in treatment of benign strictures. Often times, RBESs are narrow and torturous in which case the small delivery system of the FC-SEMS allows for better access and treatment of RBESs than the Polyflex. Three studies showed success with Alimaxx-ES ranging from 21 to 100%, with high rates of stent migration (35-39%).18-20 Bakken18 followed 56 patients with esophageal strictures. Stent migration was seen in 35.6% of patients. They correlated the propensity for stent migration to the cause and to the site of stricture. Stents migrated more frequently if strictures were caused by surgical anastomosis (60%), nonradiation (50%) and radiation (25%). Stents also were found to migrate more
Fully Covered Esophageal Stents

(continued from page 42)

frequently if the stricture was more proximal (46%) than distal (38%). This study was helpful in that it reviewed the potential factors that contribute to stent migration. Newer FC-SEMS with more flared ends (“dog bone” design) used in benign esophageal disease were found to cause a 90% improvement after stent deployment in dysphagia with 26% stent migration. This lower rate of migration may be due to improved stent design. The stents were successfully removed in 29/31 patients, suggesting that while the flare ends help keep the stent in place, they do not interfere in stent removal.

The data obtained from these small case series confirms that FC-SEMSs are removable, however suggests that while their use in treatment of RBESs is promising, more research into stent design is needed to ensure reduction in stent migration.

Esophageal Perforation and Leaks

Esophageal perforations tend to occur after endoscopic dilations or mucosal resections, whereas leaks tend to occur at sites of surgical anastomoses. Surgery is currently the gold standard of therapy. However, many times, patients with these conditions are poor surgical candidates given their age and co-morbid conditions. In these cases, endoscopic stenting has emerged as an alternative treatment. Recently, malignant of esophageal fistulas and perforations via stent placement has been demonstrated to be effective. Since endoscopic methods allow for minimally invasive and faster means of therapy when compared to surgery, use of fully covered stents in the management of benign esophageal leaks and perforations has become increasing popular. Other major advantages of endoscopic options over surgery are a shorter hospital stay, easy accessibility if perforation is recognized during or after an endoscopic procedure and the possibility for early oral intake after stent placement. While in theory it seems more practical to use endotherapy over surgery, there are no major prospective randomized studies comparing the two options. The data that does exist comes mostly of retrospective reviews. One recent review of 125 patients found that those treated with stents had a lower mortality rate in comparison to those who underwent surgery. This section will discuss several small case studies, which have evaluated the use of fully covered plastic and metal stents in the treatment of benign perforations, leaks and fistulas.

Figure 1. Endoscopic image of a Self Expanding Plastic Stent, the Polytex stent (Boston Scientific, Natick MA). The Polytex stent is fully covered and is easily removable. (Image courtesy of Douglas G. Adler MD)

Fully Covered Self Expanding Plastic Stents

Esophageal perforations and leaks are a very challenging clinical scenario with mortality rates of 20 to 45% if left untreated. With the introduction of SEPSs, clinicians have been able to treat leaks and perforations quicker and more efficiently via endoscopy. Several small studies have documented the success of SEPSs in the treatment of esophageal leaks and perforations. Freeman and colleagues reported 17 patients with esophageal perforations who underwent immediate stenting with SEPSs. The perforation was successfully sealed in 16 of 17 patients. Even more impressive, 14 of the 17 patients were able to eat within 72 hours. Tuebergen et al. followed another series of patients with esophageal perforations, of whom over half had failed initial attempts at surgical closure. They found that of their 32 patients, 78% had functional sealing while 70% had successful closure of the wall perforation with SEPSs. Another small prospective study followed patients who underwent Polytex stent placement for postoperative esophageal leaks. Among the 18 patients, leak occlusion was successful in 16. However, there were 9 cases of stent migration. In another study, 9 patients were treated with Polytex for leaks secondary to surgical resection or esophageal perforations. Sealing of the leak was achieved in 7 of the 9 patients. Stent migration did occur in 30% of the patients, however all stents were repositioned without complications. All in all, the studies based on the use of SEPSs in...
the treatment of esophageal perforations and leaks are encouraging as successful closure was achieved in the majority of patients.

**Fully Covered Self Expanding Metal Stents**

Recent interest has focused on the use of fully covered SEMSs in the endoscopic treatment of benign upper gastrointestinal leaks and perforation.30 Siersema31 treated 11 patients with traumatic esophageal perforations with a fully covered SEMS within 60 hours of diagnosis. Of the 11 perforations, 10 sealed with stenting alone. Another study followed patients with benign spontaneous or iatrogenic esophageal perforations that were treated with fully covered stents. This study had two groups; group 1 was treated within 45 minutes, while group 2 was treated with a median delay of 123 hours. All patients in group 1 had uneventful recovery and were soon discharged from the hospital. Of the group 2, 7 of 8 perforations healed; however the clinical course was much more complicated and the hospital stay much longer.32 Johnsson and colleagues33 followed 13 patients with perforations and successfully sealed the perforation in 12 of the 13 cases. All fully covered SEMSs were removed without complications. Through these studies, it appears that SEMSs are an excellent treatment modality in the management of esophageal leaks and perforations. They allow prompt treatment in the least invasive manner possible. Ongoing research will likely clarify which patients are best treated with surgery and which patients should undergo stenting.

**Esophageal Fistula**

Similar to perforations and leaks, stents have also been used to treat benign esophageal fistulas. Nonmalignant tracheoesophageal fistulas most commonly result from a complication of intubation.34 Not many studies have been done on the treatment of nonmalignant tracheoesophageal fistulas, but of the few, the options are either surgery or stenting. One study evaluated the use of partially covered SEMSs to seal esophageal fistulas in 12 ventilated patients. Fistula occlusion was achieved in every case without any complications.35 In another study of patients with RBES who also had fistulas, SEPS closed the fistulae in 68% of patients.12 Due to the limited data available, it is difficult to assess the use of fully covered stents in esophageal fistulas.

**CONCLUSION**

Esophageal stents remain highly useful in the palliation of malignant esophageal disease. With the introduction of the fully covered SEMSs and SEPSs, the application of esophageal stents has broadened to include benign esophageal diseases such as strictures, perforations, leaks and fistulas. The fully covered stents with their potential for removability have revived interest into using minimally invasive techniques to treat conditions that would otherwise require surgery. Currently, the
Fully Covered Esophageal Stents

References

35. research consisting of small retrospective case series regarding the use of FC-SEMSs and SEPSs for esophageal leaks and perforations is very encouraging. However, their use in benign esophageal strictures needs further research as the risk of stent migration is well documented. Hopefully after design modifications, fully covered esophageal stents will become the first line option for treatment of many benign esophageal conditions.