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Endoprosthetics for malignant esophageal disease

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ABSTRACT

Currently used stents for malignant esophageal strictures include self-expanding metal stents (SEMS), self-expanding plastic stents (SEPS), and biodegradable stents. For the palliative treatment of malignant dysphagia, both SEMS and SEPS effectively provide rapid relief of dysphagia. SEMS are preferred over SEPS as randomized controlled trials have shown more technical difficulties and late migration with plastic stents. Despite specific characteristics of recently developed stents, recurrent dysphagia due to food impaction, stent migration, and both tumoral and nontumoral tissue overgrowths are common. Complication rates are probably also affected by stent "behavior" in the esophagus, with radial and axial forces being important determinants. The efficacy of stents with an antireflux valve for patients with distal esophageal cancer has not convincingly been proven. Concurrent treatment with chemotherapy and radiotherapy seems to be safe and effective, although biodegradable stents have shown disappointing results. It can be expected that removable stents will increasingly be used as bridge to surgery to maintain luminal patency during neoadjuvant treatment.

1. Introduction

With 80,000 new patients and 400,000 deaths each year, esophageal cancer is the eighth most common malignancy worldwide and sixth on the list of cancer-related causes of mortality [1]. Owing to a rapid increase in the incidence of esophageal adenocarcinoma [2], esophageal cancer is also the fastest rising of all solid malignancies. As dysphagia, the predominant symptom in esophageal cancer, only occurs when more than half of the esophageal lumen is obstructed, more than 50% of patients already have incurable disease at the time of diagnosis [3-5]. The main therapeutic aim in this advanced stage should be to provide a minimally invasive and rapid relief of dysphagia. Available treatment options can be divided into endoscopic (stent placement, laser therapy, dilation or nutritional support by a nasogastric or nasoenteral tube, or percutaneous endoscopic gastrostomy) and nonendoscopic modalities (external beam radiotherapy, intraluminal radiotherapy [brachytherapy], chemotherapy, or a combination of these) [6]. Among the endoscopic treatment options, the development of esophageal endoprostheses has been rapid and currently has an established role in the treatment of dysphagia due to a malignant esophageal stricture. This review provides an overview of the latest developments in esophageal endoprostheses used in patients with malignant esophageal strictures.

2. An overview of the different types of endoprostheses

The current variety of commercially available stents can be roughly divided in fully covered and partially covered self-expanding metal stents (SEMS) and fully covered self-expanding plastic stents (SEPS). Recently, uncovered self-expandable biodegradable stents were added to this portfolio. Figure 1 depicts all the currently commercially available self-expanding stents.

The optimal stent design must be pliable and atraumatic, but at the same time, it should be strong enough to maintain luminal patency and maintain its position in the esophagus. However, stents should also be easily removable and without any risk for benign hyperplastic or malignant tumor ingrowth or overgrowth [7,8]. It may not be surprising that this ideal stent, one that combines all these characteristics, has not yet been developed.

All currently available SEMS are made of nitinol, a nickel and titanium alloy. Nitinol is known for its shape memory, which is the ability to undergo deformation at one temperature and then recover its original, undeformed shape on heating above its "transformation temperature."

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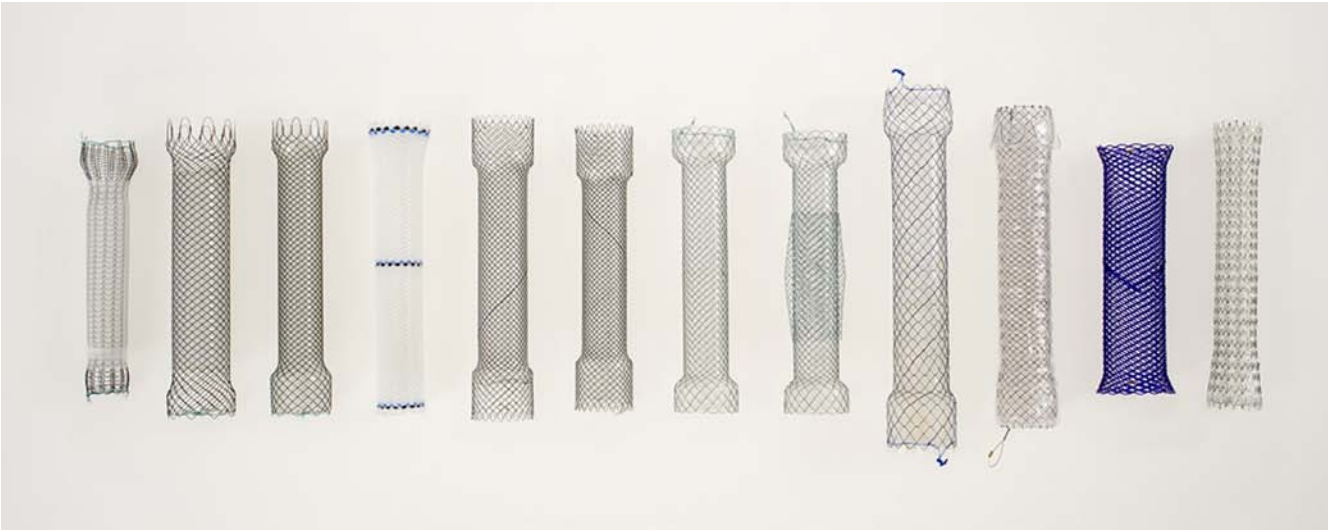

Fig. 1. An overview of self-expanding stents from left to right: the specially knitted Ultraflex stent; the small- and large-diameter partially covered Wallflex stents; the polyester Polyflex stent; the small- and large-diameter braided, partially covered Evolution stents; the single- and double-layered Niti-S stents; the Hanaro stent; the braided Ella-HV stent; and the laser-cut Alimaxx stent. (Color version of figure is available online.)

2.1. Partially covered metal stent

Partially covered SEMS have been on the market for the longest time, with the Ultraflex (Boston Scientific, Natick, MA) being the most established, still commercially available metal stent. The partially bare metal stent is known to cause a mucosal response resulting in hyperplastic tissue, which generally ensures firm stent embedding. This (nontumoral) tissue may occur in the first few weeks after stent placement. The occurrence of hyperplastic reaction is suggested to be related to radial force of the esophageal endoprosthesis but not to previous radiotherapy or chemotherapy [9]. The downside of this tissue reaction is that it can also cause recurrent dysphagia (10%-36%) [4,5]. In addition, stent removal may also be challenging [10]. However, newer partially covered stents such as the partially covered Evolution (Cook Medical, Limerick, Ireland) and the Wallflex (Boston Scientific, Natick, MA) have shown less nontumoral tissue response (14% and 10%, respectively). Surprisingly, migration rates were also lower (5% and 6%, respectively), which suggest that other factors such as stent diameter and stricture location may also be involved in preventing stent migration [11,12].

2.2. Fully covered metal stents

In the past few years, several fully covered SEMS have become available, such as the Alimaxx (Merit Medical, South Jordan, UT), the Niti-S (Taewoong Medical, Seoul, Korea), the SX-Ella (Ella-CS, Hradec Kralove, Czech Republic), the fully covered Wallflex (Boston Scientific, Natick, MA), and the fully covered Evolution (Cook Medical, Limerick, Ireland) (Figure 2). The fully covered designs are supposed to reduce recurrent dysphagia due to both hyperplastic and tumoral tissue overgrowth. As the complete covering prevents stent embedding, these stent designs are marketed as removable and theoretically may be more suitable for benign strictures. Unfortunately, migration rates are higher with fully covered stents, which consequently may lead to repeat endoscopies and recurrent dysphagia. In single-center, non-randomized case studies, migration rates in malignant strictures varied widely from 3%-10% for fully covered Evolution and the Wallflex stents, to 36% for the Alimaxx stents [13-15]. The fully covered SX-Ella stent, which was especially developed with an antimigration collar, also had a 14% migration rate [16].

Tissue reaction also varied between various studies in which the efficacy and safety of fully covered SEMS were evaluated. Patients who received a fully covered Wallflex stent for a malignant stricture rarely developed tissue reaction ($n=2$) [14] whereas in 41% of patients, relatively high rates of moderate to severe granulation tissue were reported after removal of an Alimaxx stent [15]. Although these studies are hampered by their nonrandomized design, it suggests that the fully covered design by itself does not sufficiently explain migration rates and tissue response.

2.3. Fully covered plastic stent

The Polyflex stent (Boston Scientific), fully covered with an encapsulated monofilament braid made of polyester, is the only plastic stent available. This stent was originally thought to give less tissue reaction owing to the use of plastic material instead of nitinol and that the fully covered design would ensure safe stent removal. Therefore, this stent is the only stent that is Food and Drug Administration approved for the treatment of benign esophageal strictures. However, the results were somewhat disappointing for both benign and malignant strictures [4,17-19]. Major complications such as bleeding or perforation were not absent [5], sometimes even with a fatal course in patients with benign strictures [17]. Migration rates were comparable or worse as compared with SEMS when used for both benign and malignant strictures (13%-29%) [4,5,17,18]. Furthermore, the stent has to be loaded into the introducer before placement, whereas commercially available SEMS are delivered preloaded. Lastly, the substantially larger diameter and less flexible SEPS introducer catheter more commonly requires dilation (up to 14 mm) to accommodate stent insertion [5].

2.4. Uncovered biodegradable stents

A few years ago, a biodegradable self-expandable stent, the Ella-BD stent (Ella-CS, Hradec Kralove, Czech Republic), was introduced (Figure 3). This stent is made up of poly-L-lactic acid monofilaments that dissolve over a period of 2-3 months, which confers the advantage that stent removal is not required, making them particularly useful for patients with benign strictures [20-22]. The uncovered design allows stent embedding into the