Int J Clin Exp Med 2021;14(7):2054-2066
www.ijcem.com /ISSN:1940-5901/IJCEM0123788

Review Article

Esophageal stent types and clinical applications

Tan Wang[1], Haipo Cui[1], Yinlin Shao[2], Hexuan Jiang[1], Yue Dong[1], Runtian Guo[1]

[1]*Shanghai Institute for Minimally Invasive Therapy, University of Shanghai for Science and Technology, Shanghai 200093, China;* [2]*Shanghai Putuo People's Hospital, Shanghai 200060, China*

Received October 9, 2020; Accepted February 3, 2021; Epub July 15, 2021; Published July 30, 2021

Abstract: Objective: This study aims to explore the clinical effects and material characteristics of the different types of esophageal stents and reviews the common clinical complications and contraindications. Method: We searched articles related to the clinical effects of the different types of esophageal stents in PubMed and Web of Science from their inception up to September 30, 2020. Reproducible studies were excluded, and a total of 82 articles were ultimately included. Result: Esophageal stent implantation can quickly relieve obstruction symptoms and has a high clinical effectiveness. Currently, five types of esophageal stents, i.e. self-expanding metal stents (SEMS), SEMS with an anti-reflux valve, drug-eluting and radioactive SEMS, self-expanding plastic stents, and biodegradable stents, are widely used. The common clinical complications after stent implantation include retrosternal pain, stent displacement, hemorrhage, perforation, esophageal restenosis, and so on. Conclusion: Different kinds of esophageal stents have their own advantages and disadvantages in the treatment of esophageal stenosis. Self-expanding metal stents have good histocompatibility and excellent elasticity. Anti-reflux stents significantly lower the incidence of reflux. Self-expanding plastic stents rarely induce granulation tissue reactions and result in less tissue inflammation. Drug-eluting and radioactive SEMS relieve dysphagia while inhibiting tumor cells and prolonging patient survival, so they are thought to be an optimal treatment for malignant strictures. Biodegradable stents have a great potential on account of the advantage of avoiding removal.

Keywords: Esophageal cancer, esophageal stents, esophageal stenosis, complications

Introduction

Esophageal cancer accounts for a large proportion of cancers. According to published data, there were 572,000 new cases of esophageal cancer and 509,000 deaths worldwide in 2018, with the morbidity and mortality ranking the seventh and sixth respectively among all malignant tumors [1]. The high mortality signifies that almost 1 in every 20 cancer deaths is caused by esophageal cancer. The incidence of esophageal cancer is usually three to four times higher in men than in women [2]. Early esophageal cancer can be treated by surgical resection, but the detection rate of esophageal cancer is low because of the symptoms of esophageal cancer at this stage are not obvious, so the diagnosis and treatment rate is low. More than 90% of patients with esophageal cancer are in the middle and advanced stages at the time of diagnosis, and more than 50% of patients may have metastasized at the time of diagnosis [3], losing the opportunity for radical surgical resection. Dysphagia is one of the main symptoms of esophageal cancer. To improve the quality of life and relieve patients' symptoms while reducing the morbidity and the hospital stay durations, esophageal stents have become the primary palliative therapy for dysphagia [4]. Early esophageal stents were made of hard plastic [5], and they were not well accepted because of their high complication rate. In 1983, Frimberger first reported the success of using metal stents in the treatment of esophageal stenosis, which started the era of using stents for palliating malignant dysphagia and provided a new strategy for the treatment of esophageal stenosis. Initially, stents were used only to relieve obstructions and were clinically effective. With the technological innovations and progress, coated stents, polyester plastic stents, and anti-reflux stents emerged one after another. Nowadays, stents have been widely used in benign and malignant esopha-

Figure 1. Rigid plastic esophageal stents [8].

geal strictures, esophageal fistula repair, and other esophageal diseases. Among them, drug elution and radioactive stents can relieve obstructions, while local chemotherapy and radiotherapy, and biodegradable stents can avoid removal. These two types of stents are expected to become the hot spots of future development due to their unique advantages. This paper gives a detailed review of esophageal stents and summarizes the material characteristics, clinical application effects, common clinical complications, and solutions of the different types of esophageal stents, providing information for the research and improvement of esophageal stents.

Types of stents

Rigid plastic esophageal stents

More than 100 years ago, attempts to use a hollow tube as a stent to relieve dysphagia began. In 1845, a French surgeon cured malignant esophageal strictures using a hollow tube made of decalcified ivory [6]. A similar operation was also performed by a British surgeon. However, these trials both failed. The first successful esophageal stenting was done by Symonds in a 43-year-old pregnant woman who had difficulty swallowing during pregnancy and was performed at the London Hospital in 1885 [7]. He made a six-inch stent out of tubing (number 10) and designed a funnel at the proximal with gum elastic and a conical distal end. One end of silk thread was attached to the funnel. The other end of the thread came out of the patient's mouth and was tied to the patient's ear to prevent migration after placement. The patient was ambulatory and could swallow semiliquids during the treatment. Hence, the stent not only saved this patient from undergoing a major surgery but it also helped in relieving dysphagia and thereby preventing aspiration and allowing nutrition via natural per-oral swallowing. This was the beginning of an era in which stents were used to palliate malignant dysphagia.

Several centers then started making their own stents with unique designs for the market, but the basic design remained the same: with a funnel at the proximal end, a body of different lengths, usually 18 mm in diameter, and a cone at the distal end (**Figure 1**). These stents need to be predilated before implantation, and this was usually done by locating the stenosis through fluoroscopy or endoscopy. These stents proved highly effective at relieving dysphagia. The technical success in placing these stents has been variously reported to be no less than 80% or even more than 90%. The functional success, namely, the patient's ability to eat, is greatly improved. But the rigidity of these stents means that they were not suitable for tortuous strictures. Additionally, many complications occurred, such as severe chest pain, migration, food impaction, bleeding, ulceration, new fistulas, and reflux and aspiration. And the rate of these complications was worrisome and alternative approaches were actively being researched.

Self-expanding metal stents (SEMS)

Many kinds of self-expanding metallic stents have been widely used in the treatment of esophageal cancer [9, 10]. Two types of self-expanding metal stents are available currently. One is the traditional stainless steel stent, and the other are stents made of nickel titanium metal alloy. The Wallstent and Z-stent are representative of the traditional stainless steel stents. The Wallstent was designed by Swedish scientist Hans Wallsten in 1983 [11], and it is a mesh tubular structure made of stainless steel alloy wire. It was the first self-expanding metal

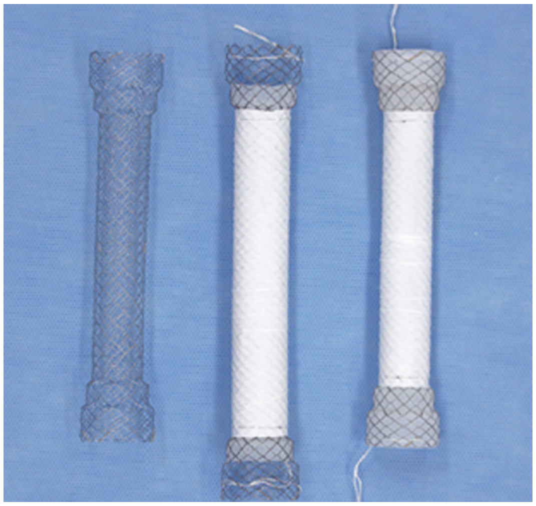

Figure 2. Uncovered SEMS (left), partially covered SEMS (middle), and fully covered SEMS (right) [13].

stand for the esophagus. Its basic structure is a dumbbell without a membrane, and the improved structure is an open trumpet with a polyurethane membrane in the center and no membrane at either end. It has a strong anti-external pressure and is not easy to deform, but it cannot be adjusted or recovered after its release. Also, the Flamingo Wallstent [12] was designed for the special structure and physiological characteristics of the lower esophagus and cardia. The stainless steel wire of the z-type stent is arranged in the shape of a "Z", with strong support, excellent plasticity, good structural compliance, and it can adapt to the bending deformation of the lesion site. The stent is covered with high-strength medical silicone rubber film and a silicone rubber skirt at the upper and lower mouths, which can prevent the tumor tissue from growing in and causes little mechanical stimulation to the adjacent tissue. It is recycled and generally used for the treatment of benign stenosis. However, the disadvantages of these two kinds of stents are poor histocompatibility, which tends to lead to significant inflammation and fibrosis of the esophageal tissues.

Currently, the most commonly-used stents in clinical applications are made of a nickel titanium metal alloy, and they have a morphological memory effect. Compared with stainless steel, the material has better histocompatibility, excellent elasticity, moderate strength, and a special softness. Esophageal strictures can be placed within a delivery device that can be compressed to less than 4 mm. Through continuous improvement and development, this kind of stent is available in three main types: covered, partially covered, and uncovered (**Figure 2**). Although the three types of SEMS have been widely used clinically, the complications that they caused were distinguishing. A variety of studies have reported that the conventional uncovered SEMS caused complications, such as fistulae, bleeding, embedment, recurrence of the tissue growth, and so on [14]. The main complication is tissue regeneration to the mesh so that the stent is inserted into the tumor tissue, leading to a new stenosis or obstruction. In bare SEMS, about 17-36% showed tumor ingrowth or overgrowth according to the study [15]. In order to solve the complications of tumor and granulation tissue growth, a variety of polymer coated materials were developed to completely cover the stent. The covering polymer materials are mainly polyester, silicone rubber, polyethylene, and so on. However, new complications occur after the covering. The covered SEMS became prone to migration because of the smooth covering structure [16], leading to the need for secondary surgery to take out the stent from stomach. The most common complication of fully covered SEMS was migration (36.3%), followed by pain and obstruction [17]. To prevent the stent migration, partially covered SEMS began to appear. The middle part of SEMS is covered but the proximal and distal ends of SEMS are exposed to allow embedding into the esophageal wall, thus reducing the incidence of stent migration. The disadvantage is that it increases the difficulty of recycling and the risk of restenosis. An interesting solution for migration, the stent was anchored to the esophageal wall via an endoscopic suturing device [18]. Benjamin et al. reported in their randomized controlled trial with 101 patients that endoscopic suturing of FC-SEMSs for benign esophageal disease reduces clinically significant stent migration compared with unsecured FC-SEMSs [19]. In another interesting method, the manufacturer designed a double-layer stent, with an exposed outer layer to prevent the stent from shifting and a fully covered inner layer to prevent the tumor from embedding. Hussain's meta-analysis showed that the displacement rate of the double-layer stents was only 4.7%, and the tumor embedding rate was only 11.2%, showing a good development prospect [20]. In general, three types of SEMS have common complications such as stent migration and tumor tissue ingrowth. The differences in the migration rates among the various SEMS are not statistically significant [21].

SEMS with an anti-reflux valve

For patients with lower esophageal and cardiac tumors, the incidence of gastroesophageal reflux and the related complications after SEMS implantation ranges from 20% to as high as 80% [22-25]. There was a recognition of the need for an SEMS that would not only relieve dysphagia but also reduce acid reflux and its related complications, especially when the patient is lying supine. Hence, anti-reflux stents with one-way valves, rotators, or valves have emerged that are effective at preventing reflux and, to a certain extent, at preventing fibrous connective tissue from growing in from the lower edge of the stent [24, 26]. Sabharwal [27] reported that there was no significant difference in the reflux rate between SEMS with an anti-reflux sleeve and conventional SEMS used in conjunction with a high-dose proton pump inhibitor (14% vs. 8%; P=0.650). Coron et al. [28] reported in their study that SEMS with an anti-reflux valve is effective in preventing reflux, but at the cost of an increased incidence of complications such as migration and/or obstruction of SEMS (55% vs. 18%; P=0.020). These results suggest that the efficacy and safety of several SEMS with anti-reflux valves available currently were difficult to evaluate due to the studies' small sample sizes and the variability in the anti-reflux features. Hence, the routine use of SEMS with anti-reflux features cannot be recommended. Further studies are needed to determine whether anti-reflux features can reduce the risk of gastroesophageal reflux.

Drug-eluting and radioactive SEMS

Drug-eluting stents and radioactive SEMS can also be used to treat cancer locally with chemotherapeutic drug membranes or radioactive particles, in addition to relieving dysphagia. Drug-eluting stents (DESs) are widely used in the vascular and bile duct fields [29], but for non-vascular organs such as the esophagus, DES has been slow to develop, and there is no clinical use of drug-eluting stents to treat esophageal cancer [30]. Drug-eluting stents can carry chemotherapy drugs such as paclitaxel, docetaxel, fluorouracil, and rapamycin on the surfaces of the drug-eluting stents [31-34]. While improving food intake, stents have the effect of anti-tumor growth and reducing mucosal tissue hyperplasia, serving as the clinical purpose of chemotherapy. This kind of localized continuous delivery system combined with the stent is a promising strategy for the treatment of malignant esophageal cancer. The stent has achieved certain effects in animal experiments. Fan et al. evaluated the efficacy and safety of paclitaxel eluting stents using a rabbit esophageal cancer model [35]. Their studies showed that in the 22 rabbits, compared with the SEMS groups, the average tumor volume and tumor areas of the drug-eluting stent groups were significantly reduced. This brought a hopeful clinical trial and a potential application. But determining the dose of the drug is and how to control the release mode and release time of the drug is still technically difficult. To further study the unidirectional controlled release drugs and to improve the mechanical properties of stents, researchers began to study a series of new films featuring multilayered structures.

Tian developed multilayer membranes based on a series of poly(caprolactone) (PCL) and polyethylene glycol polymers, which contained anti-tumor 5-fluorouracil [36]. The covering film consisted of a backing layer that blocks the release of anticancer drugs to the stomach and a multi-layer drug layer on the surface, with different concentrations of drugs in different layers to achieve a one-way controlled release of drugs. This multilayer film provides an attractive polymer-covered stent for the localized treatment of stenosis or the occlusion of esophageal cancer. Similarly, Guo's research team has developed a bilayered polymer film loaded with paclitaxel or 5-fluorouracil to treat unresectable cancer in a porcine model [37, 38]. The bilayered polymer film consists of a layer of 50% PTX or 5-FU and a layer of drug-free backing. Their results suggest that the esophageal concentrations of the drug were the highest compared with other organs. The new stent not only relieved the dysphagia, it also provided a functional local drug delivery device for esophageal cancer. These results suggest that this type of drug-eluting stent has the potential to improve and inhibit the growth of esophageal tumors.

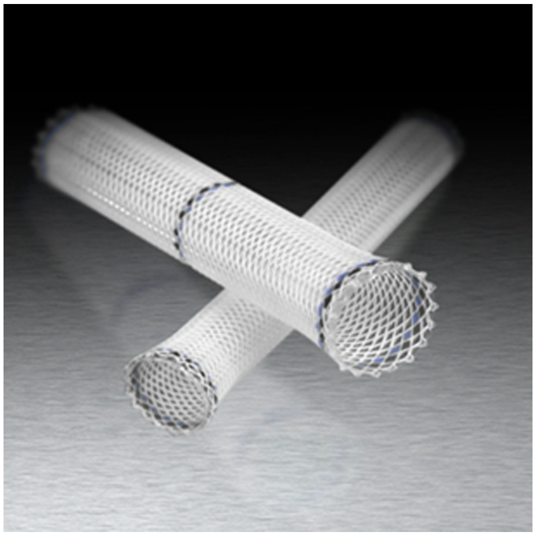

Figure 3. A self-expanding plastic esophageal stent (Polyflex stent, Boston Scientific, USA).

Radioactive SEMS are a preferred treatments for advanced esophageal cancer. The stents can carry I^{125} radioactive particles, providing radiotherapy for esophageal tumors while rapidly relieving dysphagia. Compared with ordinary external radiotherapy, radioactive SEMS can directly act on esophageal tumors, avoid dose attenuation caused by distant irradiation, and increase the dose of the radiation in the target area, thus improving the efficacy. Multicenter randomized controlled clinical trials have confirmed that I^{125} radioactive SEMS are safer and more effective than ordinary esophageal stents, significantly extending patient survival [39-45]. However, there is no consensus on the size of the particles to choose, the total dose of the particles, or how to distribute them. If the stent placement is inaccurate or the stent is displaced, it will fail to achieve the therapeutic purpose of esophageal tumors and cause collateral damage to the normal esophagus and the adjacent tissues. Meanwhile, with continuous irradiation from the I^{125} particles on the tumor cells, local stenosis caused by tumors can be improved to varying degrees, further increasing the risk of scaffold displacement.

Self-expanding plastic stents (SEPS)

Initially, since the self-expanding metal stents that were available in the market were either totally uncovered or partially covered, the bare metal wires in the SEMS could easily cause tissue damage. Moreover, the contact and friction between the tissue and the bare metal wire would easily lead to granulation tissue hyperplasia, thus causing restenosis and difficulty in extraction. These limitations demonstrate that self-expanding metal stents are not the preferred treatment for benign stenosis. So researchers began to set their sights on self-expanding plastic stents.

Self-expanding plastic stents were made of polyester plastic mesh and covered with a silicone membrane [46] (**Figure 3**). The upper opening of the bracket is large and bell-shaped to reduce displacement. The inner diameters of the middle and distal openings of the bracket are the same. When placing the stent, the barium line is placed at both ends and in the middle of the stent to facilitate X-ray examination and positioning, and to facilitate endoscopic examination of the corresponding barium line position. The stent is marked with blue. A series of prospective and multicentric studies suggests that SEPS are competitive with metal stents, with a similar efficacy but a lower cost [47-51]. Compared with SEMS, SEPS have good histocompatibility, rarely induce granulation tissue reactions, cause less tissue inflammation, and any restenosis complications at both ends of SEPS are much less likely to occur. Besides, the full covering on the stent prevents tissue growth into the stent and reduces esophageal restenosis, and it is easy to remove.

Because SEPS will not cause significant tissue damage, good therapeutic effects have been achieved in both benign and malignant esophageal stenoses, esophagotracheal fistulas, and postoperative anastomotic fistulas [52-56]. However, SEPS cannot be compressed due to the limitation of the material, and because the diameter of the conveying system is significantly increased (12~14 mm), so pre-expansion is required first. Prominent problems with SEPS include severe chest pain because of excessive radial dilatation and stent migration due to poor stent placement [57]. Conio et al. performed a prospective controlled trial to compare a new self-expanding polyester mesh stent (Polyflex) with SEMS (Ultraflex), and their study found that significantly more complications, especially late stent migration, were observed in the Polyflex group [58]. Hence, SEPS were not often used for malignant esophageal strictures, but it is the only FDA-approved self-expanding stent for benign esophageal strictures. The advantages and disadvantages of the different types of stents are listed in **Table 1**. Finally, the selection depends on the actual situation.

Biodegradable self-expanding stents

Due to the significant disadvantages of the metal and plastic stents used in benign esophageal stenosis, biodegradable stents were developed to reduce the complications. Stents made of degradable synthetic polymers were degraded and absorbed by the body within a pre-determined period of time after they achieved the therapeutic effect, which eliminated the need for removing the stents. Two stents are currently available: ELLA-Cs stents with polydioxanone braid and PLLA stents.

PLA has already been used in clinical practice such as with surgical sutures, the controlled release of drugs, with endovascular stents, and as a fracture internal fixation material. The good histocompatibility, non-toxicity and degradability of PLA have long been proved clinically. In 2006, Tanaka et al. reported a new PLA degradable stent, which consists of knitted PLLA monofilaments, and its length and diameter can be designed according to the patient's esophageal lesions. The radial strength of the support was more advantageous than the common metal support on the market at that time [59]. Saito and his team wove poly-l-lactic acid (PLLA) monofilaments into an Ultraflex-type stent and used the degradable stent to treat 13 patients with various esophageal diseases, including esophageal cancer. They found that no restenosis symptoms were observed during the follow-up of 7 months to 2 years [60]. There is also no need for further balloon dilation therapy or the replacement of biodegradable stents. However, some patients (10/13) experienced stent spontaneous migration within three weeks after the stent placement. At the same time, the same research group continued to use PLLA stents in the treatment of two patients with benign esophageal stenosis, and the results showed good postoperative healing and no signs of restenosis symptoms within six months. Therefore, PLLA stents provide a new possibility for the treatment of benign esophageal stenosis [61].

The ELLA-CS stent is the only biodegradable stent for the digestive tract. It was approved in Europe for benign esophageal stenosis in 2007. The stent is manufactured from woven polydioxanone monofilament [62] and is available in four body diameters (18, 20, 23, and 25 mm) with lengths ranging from 60 to 135 mm [63]. The middle backbone is cylindrical, and the two ends are hemlines (**Figure 4**). The stent has radiation permeability, so there are metal markers at both ends and in the middle of the stent for appearing under the X-ray. Since the advent of Ella-CS stents, they have been used to treat a variety of esophageal diseases, including chemical corrosive stenosis [64], digestive esophagitis, anastomotic stenosis [65], and achalasia. Van Boeckel et al. conducted a trial comparing the efficacy and safety of self-expanding plastic stents (SEPSs) with the placement of biodegradable stents for the treatment of RBES, and their results showed that biodegradable stents are more effective for providing long-term relief from dysphagia and require fewer procedures than SEPSs, offering an advantage [66]. However, biodegradable stents also have their limitations. Repici et al. performed a prospective study of a cohort of 21 patients with SX-Ella stents for refractory benign esophageal strictures [67]. Their results showed that 55% still experienced symptom recurrence of tissue ingrowth, and three patients suffered severe retrosternal pain after the placement. From this series of research results we can conclude that, although biodegradable stents have the advantage of not requiring stent removal compared with SEPS and SEMS, and they are expected to become a kind of potential substitute, biodegradable stents still have some inevitable complications such as shifting and tissue regeneration [68], so further studies are needed. Additionally, the unexpected biodegradation of a stent after placement may lead to stent collapse and mechanical strength reduction, thus affecting the clinical effectiveness, a prominent problem with biodegradable stents. Studies show that the mechanical integrity of a biodegradation stent is determined by its degradation properties. The degradation process of a BD stent depends not only on the properties of the materials, but also on the size and structure of the stent, and the degradation is also affected by the surrounding environment like the temperature, the pH, and the type of

Table 1. Advantages and disadvantages of the different types of stents

	Materials	Advantages	Disadvantages
Rigid Plastic Esophageal Stents	Rigid plastic	Good strength, relieve dysphagia almost immediately, prevent tumor ingrowth.	Not suitable for tortuous strictures, high rate of complications.
Self-expanding Metal Stents	Stainless steel stent	Strong support, excellent plasticity, good structural compliance and can adapt to bending deformation.	Poor histocompatibility, tend to lead to obvious inflammation and fibrosis of esophageal tissues.
	Nickel titanium metal alloy	Better histocompatibility, excellent elasticity, moderate strength and special softness.	Uncovered and partially covered SEMS have high risk of restenosis, covered SEMS prone to migration.
SEMS with Anti-reflux Valve	Nickel titanium metal alloy	Reduce acid reflux and related complications.	Potential risk of migration and obstruction.
Drug-Eluting and Radioactive SEMS	Nickel titanium metal alloy	The effect of anti-tumor growth, reduce mucosal tissue hyperplasia, rapidly relieve dysphagia, directly act on esophageal tumors.	May cause collateral damage to the normal esophagus and tissues, potential risk of stent migration after cure.
Self-expanding Plastic Stents	polyester plastic	Low cost, good histocompatibility, less tissue inflammation and restenosis.	Require pre-expansion, having similar migration rate to other fully covered stents.
Biodegradable Self-expanding Stents	Poly(L-lactic acid) Polydioxanone	Good histocompatibility, non-toxicity and degradability, eliminated the need for removing the stents.	Unexpected biodegradation may lead to stent collapse and mechanical strength reduction.

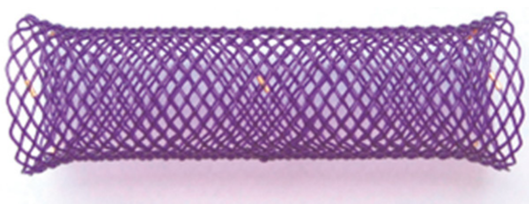

Figure 4. An SX-ELLA degradable esophageal stent [66].

body tissue/fluid. The problem that such stents need to prevent is hydrolysis before dysphagia is alleviated. Hence, further studies are needed to investigate the relationship between the degradation rate of the stent and the availability in the treatment of esophageal disease. The current evidence is insufficient, so we need more clinical cases to evaluate the relative efficacy and safety of esophageal biodegradable stents. At the same time, biodegradable magnesium alloy esophageal stents and magnesium alloy esophageal stents with anti-inflammatory (dexamethasone) and anti-proliferative (paclitaxel) compound drug coatings have also attracted attention, inspired by the application of magnesium alloy stents in the cardiovascular system.

Contraindications

Many cases were considered to be contraindications when esophageal stenting was first used. However, with the advances in stent technology and the emergence of novel stents, great progress has been made in the treatment of patients with malignant esophageal stenosis who have technical difficulties in their early treatment. Currently, there is no consensus on the absolute contraindications to stent implantation, but patients still need to choose carefully. (1) Stent placement is generally considered contraindicated in terminally ill patients with a life expectancy of <4 weeks, and in patients with distal obstructions, perforation, intestinal ischemia, sepsis, or patients with clotting disorders [69]. (2) Severe infections, coagulation disorders, cardiopulmonary complications, and other conditions that cannot be tolerated during surgery. (3) The purpose of esophageal stenting is to relieve the obstruction symptoms and to restore a normal diet. Therefore, early stenting is not recommended for patients with no significant restrictions on their food intake. (4) Cervical esophageal cancer is considered a relative contraindication due to its high displacement rate and unbearable foreign body sensation after stent implantation [70].

Complications

Esophageal stent placement complications can be classified as early or delayed. Complications that are encountered immediately or within 2-4 weeks after stent placement are called early-term complications and include retrosternal pain, foreign body sensation, migration, gastroesophageal reflux, perforation, and hemorrhage. Late-term complications are more common than the early ones and may be seen after 2-4 weeks, including migration, tumor ingrowth, food impaction and fistulas. With the development and advances in the stents and the delivery systems, early complications are decreasing. However, the delayed complications and re-intervention rates still remain a concern.

Retrosternal pain

Retrosternal pain is a common complication after stent placement, and majority of patients with esophageal stents have varying degrees of pain [9]. On the one hand, it is related to the expansion and compression of the stent that causes the tearing of the esophageal wall and local inflammation, especially after treatment using a stent in the cervical esophagus [71]. Currently, a small-diameter stent has been developed that can be placed in the cervical esophagus [72]. On the other hand, it may be caused by gastroesophageal reflux after the stent placement. Gastroesophageal reflux is mostly found in patients with lesions in the lower esophagus or the cardia. However, the occurrence of gastroesophageal reflux has been effectively controlled after the development of SEMS with an anti-reflux valve. In addition, these symptoms can be alleviated by acid-suppressing and pain-killing drugs [73] and can be removed according to the clinical conditions if necessary.

Stent migration

A series of prospective studies and literature reports have indicated that the rate of stent displacement after esophageal stent placement ranges from 0% to 40% [74, 75]. The displacement rate of various supports is also different due to the use of different materials and the mechanical dilatancy. In general, the high factors mainly include: the use of a fully covered stent, the stent diameter is too small, eating supercooled or overheated food after the implantation of nickel-titanium stents, postoperative radiotherapy or chemotherapy to shrink the tumor, insufficient expansionary force due to the hydrolysis of the degradable stent, etc. For malignant stenosis of the esophagus, stents with anti-displacement functions such as incomplete covered stents or double-layer stents are selected as much as possible according to the clinical situation to reduce the displacement rate. At the same time, endoscopic suture technology can also effectively prevent displacement [76, 77]. When the stent is placed, it can be restored or recovered under the endoscope if the stent has migrated or become detached. However, severe complications, such as severe abdominal pain, intestinal obstructions, and intestinal perforation, should be promptly removed using surgical laparotomy or laparoscopic surgery.

Hemorrhage

In general, there is a small amount of bleeding at the early stage of the stent placement, but the rate of massive bleeding requiring intervention is less than 1% [78]. Strong retrosternal pain or a foreign body sensation after the stent implantation often indicates a risk of massive hemorrhage, which should be monitored in clinical practice.

Perforation

The rate of perforation is low, and it can easily occur in the process of metal stent implantation. Multiple studies have reported perforation in <1% of patients at or after SEMS placement [79, 80]. Patients who had previously received chemotherapy and/or radiation are more likely to develop perforations. Full-thickness perforation is very rare and requires surgical management [80].

Esophageal restenosis

Studies show that the incidence of restenosis after stent placement is about 30% [81]. In some cases, the insertion of tumor tissue into the mesh of partially covered or uncovered stents will reduce the rate of stent displacement but increase the risk of stent restenosis. Another restenosis condition often occurs at the upper and lower ends of the total coated stent, resulting from the formation of tissue hyperplasia caused by esophageal peristalsis and shear force between the upper and lower mouth. It can be treated with lasers, microwaves, or argon knives using an endoscope after the restenosis, and the "stent-in-stent" technology is also an interesting approach [82].

Others

In addition, there are some less-frequent complications, but they are also reported in a large number of case statistics, such as food impaction, esophagotracheal fistulas, tracheobronchial compressed dyspnea, mediastinal organ compression, arrhythmia, fever, etc.

Summary

Esophageal cancer causes a considerable proportion of cancer-related deaths worldwide. Dysphagia is one of the main symptoms of advanced esophageal cancer, and it seriously affects patients' quality of life. Using esophageal stents for the treatment of dysphagia are the main reason that esophageal malignancies cannot be treated surgically. In 1983, Frimberger first reported on the success of metal stents for treating esophageal stenosis, which ushered in a new era of esophageal cancer stents. Then SEPS and biodegradable stents appeared. The indications for stents have also been extended from the initial malignant strictures to a variety of benign diseases. Although these stents have been used clinically for many years, there are still many unresolved complications. So we urgently need to develop novel stents to overcome the shortcomings of the existing stents.

The design of the esophageal stent, starting from the first generation of rigid plastic esophageal stents, has been slowly evolving into other types of stents in clinical applications, including self-expanding metal stents (SEMS), SEMS with anti-reflux valves, drug-eluting and radioactive SEMS, self-expanding plastic stents, and biodegradable self-expanding stents. The design principle of the stent is to relieve dysphagia and reduce the complications at the same time. As yet, there is no perfect stent such that all complications can be resolved.

The fully-covered SEMS reduces the restenosis rate, but the migration rate is higher than bare SEMS. Partially covered SEMS has better anchoring properties and less potential migration, but hyperplastic tissue reactions can easily occur. Likewise, SEPS decreases reactive tissue inflammation, but the higher rate of stent migration limits its clinical application. A SEMS with an anti-reflux valve brings the advantage of having a good effect on lower esophageal lesions. However, it still carries the risk of food obstructions. The stents currently available have their own advantages and limitations. Radioactive and drug-eluting SEMS and biodegradable stents may be the research direction of esophageal stents in the future. The advantages of radioactive and drug-eluting stents are that they relieve dysphagia while inhibiting tumor cells and prolonging patient survival. But its efficacy and safety remain to be studied. The advantage of biodegradable stents is that they don't need to be removed. However, there is still a risk of its collapse due to hydrolysis, which does not satisfy the initial assumptions of researchers. Future esophageal stents should be designed with a low complication rate and the ability to tailor them to meet individual needs at much lower cost.

Acknowledgements

This work was supported by the Shanghai Natural Science Foundation (No. 19ZR1435-300), the Shanghai Engineering Technology Research Center (No. 18DZ2250900), and the Shanghai-Yangtze River Delta Construction of Regional Innovation Community Field Project (No. 20642430100), PR China.

Disclosure of conflict of interest

None.

Address correspondence to: Haipo Cui, School of Medical Instrument and Food Engineering, University of Shanghai for Science and Technology, No. 516, Jungong Road, Yangpu District, Shanghai 200093, China. Tel: +86-21-65032249; Fax: +86-21-55270695; E-mail: h_b_cui@163.com

References

[1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA and Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394-424.

[2] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J and Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108.

[3] Sihvo EI, Luostarinen ME and Salo JA. Fate of patients with adenocarcinoma of the esophagus and the esophagogastric junction: a population-based analysis. Am J Gastroenterol 2004; 99: 419-424.

[4] Shahbaz SCM, Luketich JD, Landreneau RJ and Abbas G. Esophageal cancer: an update. Int J Surg 2010; 8: 417-422.

[5] Hill JL, Norberg HP, Smith MD, Young JA and Reyes HM. Clinical technique and success of the esophageal stent to prevent corrosive strictures. J Pediatr Surg 1976; 11: 443-50.

[6] Sw G. Gastrostomy, oesophagostomy, internal oesophagotomy, combined oesophagotomy, oesophagectomy, and retrograde divulsion in the treatment of stricture of the oesophagus. Am J Med Sci 1884; 88: 58-69.

[7] Symonds CJ. The treatment of malignant stricture of the oesophagus by tubage or permanent catheterism. Br Med J 1887; 1: 870-873.

[8] Dua KS. History of the use of esophageal stent in management of dysphagia and its improvement over the years. Dysphagia 2017; 32: 39-49.

[9] Didden P, Spaander MC, Bruno MJ and Kuipers EJ. Esophageal stents inmalignant and benign disorders. Curr Gastroenterol Rep 2013; 15: 319-327.

[10] Mangiavillano B, Pagano N and Arena M. Role of stenting in gastrointestinal benign and malignant diseases. World J Gastrointest Endosc 2015; 7: 460-480.

[11] McIntee BE. The wallstent endoprosthesis. Gastrointest Endosc Clin N Am 1999; 9: 373-381.

[12] Canic S, Ravi-Chandar K and Krajcer Z. Mathematical model analysis of Wallstent and Aneurx: dynamic responses of bare-metal endoprosthesis compared with those of stent-graft. Tex Heart Inst J 2005; 32: 502-506.

[13] Kim KY, Tsauo J and Song HY. Self-expandable metallic stent placement for the palliation of esophageal cancer. J Korean Med Sci 2017; 32: 1062-1071.

[14] Jain P. Self-expanding metallic esophageal stents: a long way to go before a particular stent can be recommended. World J Gastroenterol 2011; 17: 5327-5328.

[15] Sabharwal T, Morales JP, Salter R and Adam A. Esophageal cancer: self-expanding metallic stents. Abdominal Imaging 2005; 30: 456-464.

[16] Liang DH, Hwang E, Meisenbach LM, Kim MP, Chan EY and Khaitan PG. Clinical outcomes following self-expanding metal stent placement for esophageal salvage. J Thorac Cardiovasc Surg 2017; 154: 1145-1150.
[17] So H, Ahn JY and Han S. Efficacy and safety of fully covered self-expanding metal stents for malignant esophageal obstruction. Dig Dis Sci 2018; 63: 234-241.
[18] Yang J, Siddiqui AA and Kowalski TE. Esophageal stent fixation with endoscopic suturing device improves clinical outcomes and reduces complications in patients with locally advanced esophageal cancer prior to neoadjuvant therapy: a large multicenter experience. Surg Endosc 2017; 31: 1414-1419.
[19] Bick BL, Imperiale TF, Johnson CS and DeWitt JM. Endoscopic suturing of esophageal fully covered self-expanding metal stents reduces rates of stent migration. Elsevier Inc 2017; 86: 1015-1021.
[20] Hussain Z, Diamantopoulos A and Krokidis M. Double-layered covered stent for the treatment of malignant oesophageal obstructions: systematic review and meta-analysis. World J Gastroenterol 2016; 22: 7841-7850.
[21] Jang S, Parsi M, Collins J and Vargo J. Predictors of esophageal self-expandable metal stent migration: an academic center study. Gastrointest Interv 2016; 5: 72-79.
[22] Dua KS. Antireflux stents in tumors of the cardia. Am J Med 2001; 111: 190S-196S.
[23] Dua KS, Kozarek R and Kim J. Self-expanding metal esophageal stent with anti-reflux mechanism. Gastrointest Endosc 2001; 53: 603-613.
[24] Laasch HU. Valved esophageal stents: benefits for patients outweigh perceived risks. Gastrointest Endosc 2005; 62: 822-823.
[25] Laasch HU, Marriott A and Wilbraham L. Effectiveness of open versus antireflux stents for palliation of distal esophageal carcinoma and prevention of symptomatic gastroesophageal reflux. Radiology 2002; 225: 359-65.
[26] Shim CS, Jung IS and Cheon YK. Management of malignant stricture of the esophagogastric junction with a newly designed selfexpanding metal stent with an antireflux mechanism. Endoscopy 2005; 37: 335-339.
[27] Sabharwal T, Gulati MS and Fotiadis N. Randomised comparison of the FerX Ella antireflux stent and the ultraflex stent: proton pump inhibitor combination for prevention of post-stent reflux in patients with esophageal carcinoma involving the esophago-gastric junction. J Gastroenterol Hepatol 2008; 23: 723-728.
[28] Coron E, David G and Lecleire S. Anti-reflux versus conventional self-expanding metallic stents (SEMS) for distal esophageal cancer: results of a multicenter randomized trial. Endosc Int Open 2016; 4: E730-736.
[29] Lee DK, Kim HS and Kim KS. The effect on porcine bile duct of a metallic stent covered with a paclitaxel-incorporated membrane. Gastrointest Endosc 2005; 61: 296-301.
[30] Tokar JL, Banerjee S and Barth BA. Drug-eluting/biodegradable stents. Gastrointest Endosc 2011; 74: 954-958.
[31] Hennequin C, Guillerm S and Wong S. Endoluminal brachytherapy: bronchus and oesophagus. Cancer Radiother 2018; 22: 367-371.
[32] Shaikh M, Zhang H and Wang H. In vitro and in vivo assessment of docetaxel formultion developed for esophageal stents. AAPS Pharm Sci Tech 2017; 18: 130-137.
[33] Shaikh M, Choudhury NR and Knott R. Engineering stent based delivery system for esophageal cancer using docetaxel. Mol Pharm 2015; 12: 2305-2317.
[34] Wang Z, Liu J and Wu K. Nitinol stents loaded with a high dose of antitumor 5-fluorouracil or paclitaxel: esophageal tissue responses in a porcine model. Gastrointest Endosc 2015; 82: 153-160.
[35] Zhang Y, Gao Y and Chen J. Effect of a paclitaxel-eluting metallic stent on rabbit esophagus. Exp Ther Med 2016; 12: 2928-2936.
[36] Lei L, Liu X, Guo S, Tang M, Cheng L and Tian L. 5-Fluorouracil-loaded multilayered films for drug controlled releasing stent application: drug release, microstructure, and ex vivo permeation behaviors. J Control Release 2010; 146: 45-53.
[37] Wang Z, Liu J and Wu K. Nitinol stents loaded with a high dose of antitumor 5-fluorouracil or paclitaxel: esophageal tissue responses in a porcine model. Gastrointest Endosc 2015; 82: 153-160.
[38] Liu J, Wang Z and Wu K. Paclitaxel or 5-fluorouracil/esophageal stent combinations as a novel approach for the treatment of esophageal cancer. Biomaterials 2015; 53: 592-599.
[39] Chen HL, Shen WQ and Liu K. Radioactive self-expanding stents for palliative management of unresectable esophageal cancer: a systematic review and meta-analysis. Dis Esophagus 2017; 30: 1-16.
[40] Fuccio L, Mandolesi D and Farioli A. Brachytherapy for the palliation of dysphagia owing to esophageal cancer: a systematic review and meta-analysis of prospective studies. Radiother Oncol 2017; 122: 332-339.
[41] Tian D, Wen H and Fu M. Comparative study of self-expanding metal stent and intraluminal radioactive stent for inoperable esophageal squamous cell carcinoma. World J Surg Oncol 2016; 14: 18-25.

[42] Liu N, Liu S and Xiang C. Radioactive self-expanding stents give superior palliation in patients with unresectable cancer of the esophagus but should be used with caution if they have had prior radiotherapy. Ann Thorac Surg 2014; 98: 521-6.
[43] Zhu HD, Guo JH and Mao AW. Conventional stents versus stents loaded with (125) iodine seeds for the treatment of unresectable oesophageal cancer: a multicentre, randomised phase 3 trial. Lancet Oncol 2014; 15: 612-619.
[44] Wang ZM, Huang XB and Cao J. Intraluminal radioactive stent compared with covered stent alone for the treatment of malignant esophageal stricture. Cardiovasc Intervent Radiol 2012; 35: 351-358.
[45] Guo JH, Teng GJ and Zhu GY. Self-expandable stent loaded with 125I seeds: feasibility and safety in a rabbit model. Eur J Radiol 2007; 61: 356-361.
[46] Ott C, Ratiu N, Endlicher E, Rath HC, Gelbmann CM, Schölmerich J and Kullmann F. Self-expanding Polyflex plastic stents in esophageal disease: various indications, complications, and outcomes. Surg Endosc 2007; 21: 889-896.
[47] Bethge N and Vakil N. A prospective trial of a new self-expanding plastic stent for malignant esophageal obstruction. Am J Gastroenterol 2001; 96: 1350-1354.
[48] Conigliaro R, Battaglia G and Repici A. Polyflex stents for malignant oesophageal and oesophagogastric stricture: a prospective, multicentric study. Eur J Gastroenterol Hepatol 2007; 19: 195-203.
[49] Costamagna G, Shah SK and Tringali A. Prospective evaluation of a new self-expanding plastic stent for inoperable esophageal strictures. Surg Endosc 2003; 17: 891-895.
[50] Decker PLJ and Decker D. Use of the Polyflex stent in the palliative therapy of esophageal carcinoma: results in 14 cases and review of the literature. Surg Endosc 2001; 15: 1444-1447.
[51] Dormann AJ, Eisendrath P and Wigginghaus B. Palliation of esophageal carcinoma with a new self-expanding plastic stent. Endoscopy 2003; 35: 207-211.
[52] Radecke K, Gerken G and Treichel U. Impact of a self-expanding, plastic esophageal stent on various esophageal stenoses, fistulas, and leakages: a singlecenter experience in 39 patients. Gastrointest Endosc 2005; 61: 812-818.
[53] Schubert D, Scheidbach H, Kuhn R, Wex C, Weiss G, Eder F, Lippert H and Pross M. Endoscopic treatment of thoracic esophageal anastomotic leaks by using silicone-covered, self-expanding polyester stents. Gastrointest Endosc 2005; 61: 891-896.
[54] Adler DG and Pleskow DK. Closure of a benign tracheoesophageal fistula by using a coated, selfexpanding plastic stent in a patient with a history of esophageal atresia. Gastrointest Endosc 2005; 61: 765-768.
[55] Ott C, Ratiu N, Endlicher E, Rath HC, Gelbmann CM, Schölmerich J and Kullmann F. Self-expanding Polyflex plastic stents in esophageal disease: various indications, complications, and outcomes. Surg Endosc 2007; 21: 889-896.
[56] Adler DG, Fang J and Wong R. Placement of Polyflex stents in patients with locally advanced esophageal cancer is safe and improves dysphagia during neoadjuvant therapy. Gastrointest Endosc 2009; 70: 614-619.
[57] Pennathur A, Chang AC and McGrath KM. Polyflex expandable stents in the treatment of esophageal disease: initial experience. Ann Thorac Surg 2008; 85: 1968-1973.
[58] Conio M, Repici A and Battaglia G. 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: 2667-2677.
[59] Tanaka T, Takahashi M and Nitta N. Newly developed biodegradable stents for benign gastrointestinal tract stenoses: a preliminary clinical trial. Digestion 2007; 74: 199-205.
[60] Saito Y, Tanaka T and Andoh A. Usefulness of biodegradable stents constructed of poly-l-lactic acid monofilaments in patients with benign esophageal stenosis. World J Gastroenterol 2007; 13: 3977-3980.
[61] Saito Y, Tanaka T and Andoh A. Novel biodegradable stents for benign esophageal strictures following endoscopic submucosal dissection. Dig Dis Sci 2008; 53: 330-333.
[62] Stivaros SM, Williams LR, Senger C, Wilbraham L and Laasch HU. Woven polydioxanone biodegradable stents: a new treatment option for benign and malignant oesophageal strictures. Eur Radiol 2010; 20: 1069-1072.
[63] Iñaki II, Sonia GP, Anna N, Belén MA, Carlos SP, Bilgehan K and Rıza DA. Biodegradable stents for the treatment of refractory or recurrent benign esophageal stenosis. Expert Rev Med Devices 2016; 13: 583-99.
[64] Karakan T, Utku OG and Dorukoz O. Biodegradable stents for caustic esophageal strictures: a new therapeutic approach. Dis Esophagus 2013; 26: 319-322.
[65] Hooft JE, Berge Henegouwen MI and Rauws EA. Endoscopic treatment of benign anastomotic esophagogastric strictures with a biode-

gradable stent. Gastrointest Endosc 2011; 73: 1043-1047.

[66] Boeckel PG, Vleggaar FP and Siersema PD. A comparison of temporary selfexpanding plastic and biodegradable stents for refractory benign esophageal strictures. Clin Gastroenterol Hepatol 2011; 9: 653-659.

[67] Repici A, Vleggaar FP and Hassan C. Efficacy and safety of biodegradable stents for refractory benign esophageal strictures: the BEST (Biodegradable Esophageal Stent) study. Gastrointest Endosc 2010; 72: 927-934.

[68] Kang YQ. A review of self-expanding esophageal stents for the palliation therapy of inoperable esophageal malignancies. BioMed Res Int 2019; 2019: 1-11.

[69] Yakami M, Mitsumori M, Sai H, Nagata Y, Hiraoka M and Nishimura Y. Development of severe complications caused by stent placement followed by definitive radiation therapy for T4 esophageal cancer. Int J Clin Oncol 2003; 8: 395-398.

[70] Katsanos K, Sabharwal T and Adam A. Stenting of the upper gastrointestinal tract: current status. Cardiovasc Intervent Radiol 2010; 33: 690-705.

[71] Schowengerdt CG. Tracheoesophageal fistula caused by a self-expanding esophageal stent. Ann Thorac Surg 1999; 67: 830-831.

[72] Conigliaro R, Battaglia G, Repici A, De Pretis G, Ghezzo L, Bittinger M, Messmann H, Demarquay JF, Togni M and Blanchi S. Polyflex stents for malignant oesophageal and oesophagogastric stricture: a prospective, multicentric study. Eur J Gastroenterol Hepatol 2007; 19: 195-203.

[73] Kaltsidis H, Mansoor W and Park JH. Oesophageal stenting: status quo and future challenges. Br J Radiol 2018; 91: 1-10.

[74] Doosti-Irani A, Mansournia MA and Rahimi-Foroushani A. Complications of stent placement in patients with esophageal cancer: a systematic review and network meta-analysis. PLoS One 2017; 12: 1-18.

[75] Wagh MS, Forsmark CE and Chauhan S. Efficacy and safety of a fully covered esophageal stent: a prospective study. Gastrointest Endosc 2012; 75: 678-682.

[76] Yang J, Siddiqui AA and Kowalski TE. Esophageal stent fixation with endoscopic suturing device improves clinical outcomes and reduces complications in patients with locally advanced esophageal cancer prior to neoadjuvant therapy: a large multicenter experience. Surg Endosc 2017; 31: 1414-1419.

[77] Wright A, Chang A and Bedi AO. Endoscopic suture fixation is associated with reduced migration of esophageal fully covered selfexpandable metal stents (FCSEMS). Surg Endosc 2017; 31: 3489-3494.

[78] Na HK, Song HY and Kim JH. How to design the optimal selfexpandable oesophageal metallic stents: 22 years of experience in 645 patients with malignant strictures. Eur Radiol 2013; 23: 786-796.

[79] Sharma P and Kozarek R. Practice Parameters Committee of American College of Gastroenterology. Role of esophageal stents in benign and malignant diseases. Am J Gastroenterol 2010; 105: 258-273.

[80] Nagahama T, Maruyama M, Kato K, Shinoura H, Hasegawa K, Takashima I and Ebuchi M. Complication after self-expandable metallic stent for esophageal cancer. Gan To Kagaku Ryoho 2003; 30: 1750-1753.

[81] Kang HW and Kim SG. Upper gastrointestinal stent insertion in malignant and benign disorders. Clin Endosc 2015; 48: 187-193.

[82] Aiolfi A, Bona D and Ceriani C. Stent-in-stent, a safe and effective technique to remove fully embedded esophageal metal stents: case series and literature review. Endosc Int Open 2015; 3: E296-E299.