Unusual Applications of Metal Stents in Gastrointestinal Tract

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5.1 Introduction

Much progress has been made since Coyas deployed the first esophageal stent in a patient with a malignant esophageal stricture in 1955 [1]. Over time, many steps have been taken in the search for the most suitable material for gastrointestinal endoprosthesis: the first stents were rigid, made of materials such as rubber, ivory, sandalwood, and polyvinyl. In most cases they were "homemade."

Self-expandable metallic stents (SEMS) have been the main turning point, ensuring a widespread of these devices in the gastroenterological field, initially for the treatment of malignant esophageal strictures, subsequently of colon cancer obstruction and then in a wide variety of clinical scenarios.

SEMS consist of a mesh of braided metal wires that are assembled in a tubelike structure. They are available in different lengths and calibers, and they can be with or without coating. Physical properties of materials, texture, and shape determine the radial and longitudinal force exerted by SEMS when released. Therefore, the technical characteristics of stents must be known in order to use the most appropriate device in the various clinical situations.

The first alloy used in the construction of SEMS was stainless steel, with different percentages of iron, chromium, and molybdenum; the latter helps to stabilize the crystal structure and to determine the physical characteristics. The final process of electropolishing removes most of the elements from the metal surface leaving a high concentration of chromium; after exposure to air and sterilization, a layer of a

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few nanometers in thickness stabilizes the surface and prevents oxidation. Surface defects and trace elements can cause changes in protein and affect cellular reactions. Other materials used in the construction of stents are titanium and nitinol (nickel-titanium alloy). Titanium is a metallic element well known for its resistance to corrosion (almost as much as platinum) and for its high strength/weight ratio. It is lightweight and tough, with a low density (40 % of that of steel). When it is in the pure state, it is quite ductile, shiny, white metal. Titanium is as strong as steel but 45 % lighter. Titanium is also used as an alloy. Nitinol is instead a superelastic alloy composed of nickel-titanium, which belongs to the category of "shape memory" metals (Shape Memory Alloys, SMA). In particular, the term shape memory alloys indicates a broad class of metal alloys, discovered fairly recently, which are able to recover a macroscopic preset form, thanks to the simple change of temperature. When an SMA is below its transformation temperature, it can be deformed quite easily; however, if we heat the material above the transformation temperature, it takes over a change in the crystal structure which causes the return to the original form and develops considerable force. Moreover, they have other characteristics, such as the superelastic behavior, which has multiplied the possibilities of use and the ability to generate high forces in the recovery phase of the shape. Greater flexibility and more accurate positioning in angled segments are favored by the introduction of a heart of platinum within the nitinol wire: this material is called platinol. Another alloy called elgiloy used in the manufacture of SEMS is constituted by cobalt-chromium-nickel which gives a combination of high strength, ductility, with good mechanical properties.

The presence of coating is of great interest and determines the possibility of application of SEMS in particular clinical situations: in fact, uncovered SEMS have a greater gripping at the level of the visceral wall, but they cannot generally be removed and over time are likely to experience neoplastic or granulation tissue ingrowth within the stent meshes, with subsequent obstruction. On the other hand, fully covered SEMS are at increased risk of migration, given the reduced gripping, but can be removed and are less likely to encounter ingrowth. Moreover, they can be useful in the presence of visceral wall perforation or fistula. Partially covered SEMS are also available: they have a complete coating at the level of the body and bare ends. This type of SEMS has theoretically a lower risk of migration compared to completely coated ones and allows to exploit the cover at the level of the body, for example, to treat a defect in the gastrointestinal wall.

Currently the most widely used coating materials are polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), and polyurethane (PU, used only in few cases). PET is a polymer composed of long chains of glycol and terephthalic acid: its good expansion force derives from high dissociation energy of covalent bonds of the polymer chains. It has a high surface energy and a weaving disposed in the longitudinal or transversal space which gives elasticity. PTFE is composed of carbon chains saturated with fluorine: the final structure is somewhat rigid and chemically stable. This explains some of the characteristics of this polymer, such as the low coefficient of friction, the high melting point, and the low surface energy. These physical properties are correlated with some biological behaviors, such as small

tissue reaction. PU, unlike PET and PTFE, can be rigid or soft according to its composition. Compared to the past, polyurethanes have been abandoned by their low biodegradability; current ones have a higher biodegradability. The key features are the porosity of the material, the expansion about six times the diameter in closing, and the high surface energy.

SEMS also differ in the delivery system: currently available stents are mounted on systems that can be introduced into the working channel of the endoscope (through-the-scope, TTS) or on larger diameter catheters that go directly on guidewire (over-the-wire, OTW) and which cannot be introduced into the working channel of the endoscope. Both devices are constituted by a system of coaxial tubes in which the stent is loaded around a catheter that carries the guidewire, forced inside a shorter carrier catheter. Once this is retracted, SEMS is released from the distal end. Some systems allow instead of releasing the stent starting from the proximal flare. Another delivery system consists of a catheter on which the stent is maintained fixed with a braided suture. The prosthesis is gradually released by pulling a ring connected to the wire that allows to unravel the suture (Ultraflex esophageal or colonic stents, Boston Scientific, Natick, Massachusetts). Therefore, also the characteristics of delivery systems must be carefully considered in relation to the seat and to the characteristics of the target lesion.

Currently, SEMS with particular technical characteristics are available on the market, such as anti-reflux valves and anti-migration systems. Such devices may be used to make a more tailored endoscopic therapeutic approach to the patient.

Finally we must remember that nonmetallic stents are also available: biodegradable stents (ELLA-CS, Trebes, Czech Republic) and self-expanding plastic stents (SEPS, Polyflex, Boston Scientific, Natick, Massachusetts). These latter have found wide application in the treatment of benign esophageal strictures as an alternative to SEMS.

Enteral SEMS are a nonsurgical alternative for the palliative treatment of malignant esophageal and colonic strictures. In this chapter, we will discuss the role of SEMS in some particular clinical situations in the upper and lower digestive tract, taking into account also benign disorders, gastrointestinal perforations, and anastomotic leakages after surgery.

5.2 Unusual Application of Stents in Upper GI Tract

5.2.1 Upper Malignant Esophageal Strictures

The tumors of the cervical esophagus account for approximately 10 % of esophageal cancers, and they are commonly considered difficult to manage. The use of SEMS in the palliation of dysphagia in inoperable patients is particularly controversial because frequently stents may evoke an unbearable foreign body sensation in the pharynx. In addition, more rarely, they can cause dangerous complications such as aspiration of the bolus in the larynx, perforation or esophagotracheal fistula, or proximal migration with airway obstruction.

In 1999 Conio et al. described the use of SEMS in the palliation of dysphagia in six patients with squamocellular upper esophageal cancer. Stents were deployed within 2 cm of the cricopharyngeal muscle, under simultaneous endoscopic and fluoroscopic control. Dysphagia improved significantly in all patients. Four patients had tumor ingrowth, and three of them were successfully treated by placing a second SEMS. No patient complained of globus sensation [2]. Macdondald et al. reported 22 patients with malignant strictures of cervical esophagus treated with SEMS, which was correctly placed in 93 % of cases, among them 82 % reported no foreign body sensation [3]. Other authors reported similar results [4, 5]. A more recent study by Parker et al. compared a large group of patients with cervical esophageal cancer and a matched control group of patients with distal esophageal cancer. They found no differences in terms of clinical success, survival rate, and complication rate between the two groups [6]. Also in a large study by Verschuur et al., 104 patients with primary esophageal carcinoma or recurrent cancer after gastric tube interposition within 8 cm distance distal of the UES were treated with SEMS [7]. Twenty-four (23 %) patients also had a tracheoesophageal fistula. Technical success was 96 %, with significant improvement of dysphagia in all treated patients and fistula sealing was achieved in 79 % of cases. However, major complications (aspiration pneumonia, hemorrhage, fistula, and perforation) occurred in 21 % of patients. Persistent globus sensation was reported by 8 % of patients; however, none of them required stent retrieval [7]. In conclusion, while lacking large prospective randomized trials, the use of SEMS in the treatment of stenosis of the cervical esophagus is considered to be useful and safe in expert hands.

Though the use of large-diameter SEMS in the treatment of cervical esophageal strictures [8] has been described, we recommend the use of small caliber stents, possibly with a small proximal flare. Several SEMS were designed with specific features for this purpose [9]. The body of the stent should not exceed 16 mm in size. Smaller sizes are recommended in patients who have undergone radiation therapy, due to an increased risk of esophagotracheal fistula. Furthermore, the stent should be completely covered, in order to easily remove, in the event the patient develops a feeling of foreign body.

5.2.2 Benign Esophageal Strictures

Although the use of SEMS in the treatment of malignant esophageal strictures is considered effective, their use in benign refractory stenosis has number of issues. Benign strictures can be caused by gastroesophageal reflux disease, caustic ingestion, radiation therapy, and sclerotherapy, or they can occur on surgical anastomosis. If despite repeated sessions of dilation with bougies or balloon, dysphagia persists; SEMS become a therapeutic option. Since this is a benign disease, the stent used should be removable after obtaining the degree of expansion desired, so the choice should fall on covered or partially covered SEMS [10, 11]. Partially covered SEMS guarantee better gripping to the esophageal wall and have a lower risk of distal migration. However, studies available in the literature demonstrate a

high rate of complications with this type of stent. In particular, the most feared complication is the appearance of ingrowth of granulation tissue at the level of bare heads of the endoprosthesis [12]. In these cases, it is possible to place a fully covered SEMS inside the previous one: in this way it is possible to remove both stents after 10–14 days, because the pressure exerted by the coated stent determines necrosis of the granulation tissue [13]. As previously indicated, also self-expanding plastic stents/biodegradable stents have been widely indicated for the treatment in refractory benign esophageal strictures [14]. In a recent pooled analysis of 232 patients with refractory benign esophageal strictures treated with self-expandable stent placement, technical and clinical success resulted to be quite disappointing. Fully covered SEMS were correctly deployed in 85 % of patients, but only 14.1 % experienced a significant clinical improvement of dysphagia [15]. Also with biodegradable stents and self-expanding plastic stents, authors reported poor rate of technical and clinical success (67 %, 25 % and 77 %, 12 %, respectively) [15]. In the same study, the overall rate of severe complications was 17.7 %. Among 85 subjects treated with SEMS, five patients had severe retrosternal pain, two severe nausea and vomiting, two aspiration pneumonia, and one arrhythmia [15]. SEMS migration occurred in 31.8 % of patients treated with fully covered stents, while tissue ingrowth occurred only in 3.5 % of patients. Stent removal was planned after 4–12 weeks and was successfully achieved in 97.6 % of cases [15]. In the light of these data, we believe the treatment of benign stenosis with covered or partially covered SEMS should be considered only in those patients who are refractory to dilation and who are unfit for surgery (Fig. 5.1).

Fig. 5.1 Panorama of esophageal stent. From the *left* to the *right*: Partially covered stent (Ultraflex), Polyflex stent, Partially covered stent (Evolution), Fully covered stent (SX-Ella), fully covered stent (Niti-S antimigration), fully covered stent (Alimaxx-E stent)

5.2.3 Benign Esophageal Leakages or Fistula

Benign esophageal leakages or fistula are frequently encountered and require urgent intervention to the high risk of sepsis and the high mortality rate. Anastomotic leakage may occur in up to 10 % of patients undergoing esophageal resection. Also iatrogenic perforation or Boerhaave syndrome have been successfully treated with SEMS. As shown in Fig. 5.2, the placement of covered or partially covered SEMS constitutes an indication to treat an esophageal fistula resulting in a valid alternative to surgery, favoring the healing of the defect in the esophageal wall, the control of sepsis, and a more rapid intake of an oral diet. A recent meta-analysis of Dasari et al. reported data on 117 patients from 12 studies [16]. Technical and clinical successes were 96.5 % and 86.2 %, respectively. Stent migration occurred in 11 % of treated patients. However, five patients had a perforation induced by stent, two of them due to erosion of the wall of the aorta [16]. Endoscopic reintervention and surgical intervention were needed in 5 % and 15 % of cases, respectively [16]. In the same meta-analysis, the authors also considered patients treated with SEPS: the data show that they have a higher incidence of migration and need more frequent endoscopic reoperation, while the need for a surgical intervention does not seem to significantly differ from that of SEMS [16]. The use of SEMS in the treatment of a defect in the esophageal wall must be always taken into account: the choice of the stent must take account of the greater risk of migration in the absence of stenosis. We believe the choice should fall on large-diameter partially covered SEMS. The removal must be programmed within 4–6 weeks, in order to minimize the risk of ingrowth. Also in this scenario, the stent-in-stent technique should be considered in case of embedment [13]. It is also

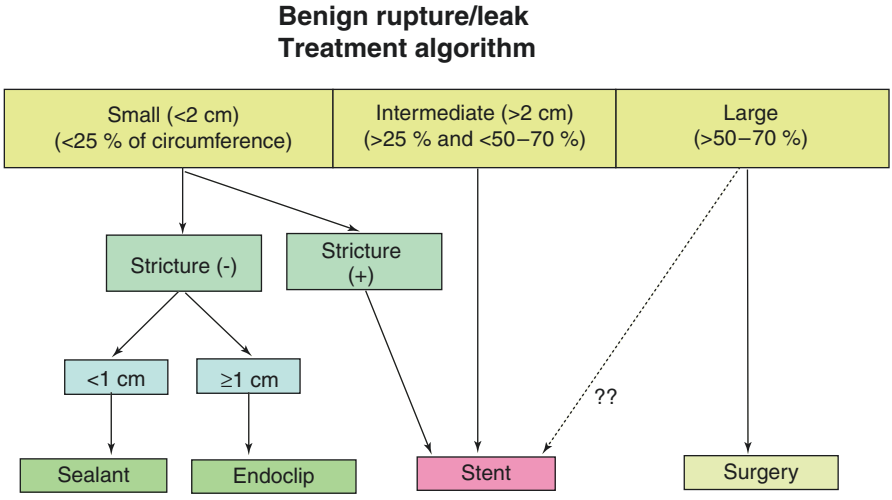

Fig. 5.2 Diagram indications to apply stents in esophageal fistula or rupture (Esophageal perforation In: Tham T, Collins J and Soetikno R, eds. *Gastrointestinal Emergencies* Oxford: Blackwell Publishing Ltd 2008)

necessary to remember that any periesophageal collection must be drained, and the patient must always be treated with broad-spectrum antibiotics.

5.2.4 Variceal Bleeding

Active bleeding from esophageal varices is considered a major cause of mortality in patients with decompensated liver cirrhosis. Treatment is currently based on vasoactive drugs, band ligation or sclerosis, and antibiotic therapy; however, they can fail in 10–15 % of patients. Tamponade balloon or the positioning of TIPSS may be proposed in these cases, however in clinical practice, TIPSS is not readily available quickly. Over the past 10 years, many cases of patients with refractory variceal bleeding treated with SEMS with excellent results have been described in literature, so that the 2015 Baveno Workshop on portal hypertension has proposed the placement of SEMS as a possible therapeutic option, awaiting further confirmations from clinical trials [17]. A review by Changela et al. showed data about 103 cases of patients treated with fully covered SEMS: Technical success rate was 97 %, with a bleeding control achieved in 96 % of treated patients. All SEMS were successfully removed after 4–14 days. Stent migration occurred in about 21 % of patients [18]. A more recent systematic review with meta-analysis took into account data on 13 studies [19]. The pooled estimate rates were 0.12 (95 % CI = 0.07–0.21) for variceal bleeding mortality and 0.18 (95 % CI = 0.11–0.29) for failure to control bleeding with SEMS [19]. The available data suggest that a proportion of less than 40 % of patients with refractory variceal bleeding dies 1 month after placement of SEMS. Therefore SEMS could be considered as a bridge therapy in selected patients undergoing other interventions such as TIPSS or liver transplantation. The choice must fall on a completely covered and large-diameter stent. The removal must be scheduled within 2 weeks, making it easier to prevent the removal of the device, reducing the risk of injury and variceal rebleeding.

5.2.5 Esophageal Achalasia

Therapeutic interventions for endoscopic esophageal achalasia include pneumatic dilation, intrasphincteric injection of botulinum toxin, and most recently the peroral endoscopic myotomy (POEM). The rate of clinical remission obtained with pneumatic dilatation, however, dramatically decreases over time from 20 to 60 % in 10 years. Temporary placement of large-diameter SEMS at the level of the cardia has been proposed as a possible therapeutic intervention in patients with achalasia. The rationale of their use is linked to the possibility to perform a gradual and prolonged dilation at the level of the lower esophageal sphincter, which, compared to traditional pneumatic dilation, should secure better long-term results.

In a study by Ying-Sheng, 90 patients with achalasia have been treated with different size SEMS: 20, 25, and 30 mm. Partially covered SEMS have been deployed across the esophageal cardia, and they were left in place for 4–5 days, before being

removed. Technical success was achieved in all patients; however, best results were obtained with larger-diameter SEMS: the treatment failure rate was lower in patients treated with 30 mm SEMS (13 %) compared to the other groups [20]. SEMS migration occurred more frequently in patients receiving 20 and 25 mm SEMS. Moreover, patients were followed up to 10 years and larger-diameter SEMS showed better long-term results [20]. Similar results have been reported also in other studies [21–23]. In another study comparing SEMS and pneumatic dilation, a temporary, 30-mm diameter SEMS was associated with a better long-term clinical efficacy in the treatment of patients with achalasia [22]. Similar better long-term outcomes have been shown in another study comparing removable SEMS and botulinum toxin injection [23]. While these data are promising, studies from Western countries are lacking, and SEMS dedicated to achalasia are not widespread used.

5.2.6 Staple Line Leaks Postlaparoscopic Sleeve Gastrectomy

The use of SEMS deserves a special mention in the treatment of staple line dehiscence after laparoscopic sleeve gastrectomy. This is the most feared complication of this surgery, providing greater morbidity. Its incidence varies depending on the series but seems to have decreased over time from 2.5 % to 1.1 % [24]. However other authors reported higher incidence of leakages up to 20 %, also in experienced hands [25]. Leakage typically develops at the esophagogastric junction and proximal stomach, near the angle of His. The cause of leakage is to be attributed to an altered healing process of the suture line, which depends on many risk factors, such as ischemia due to the devascularization of gastric wall. An increased intraluminal pressure of gastric tube has also been invoked as another mechanism involved in staple line leaks, especially if the gastric tube is little distensible or if there is a stricture of the sleeve [26]. Although it is not accepted by all, in recent years, several authors have proposed the use of fully covered SEMS in the treatment of this type of fistula with variable results [27, 28]. Only the leakages located at the esophagogastric junction or the proximal portion of gastric tube are susceptible to such treatment. SEMS migration is the most frequent complication, occurring in up to 30 % of cases. Therefore these SEMS should be as wide and as long as possible, in order to prevent dislocation. Many authors remove them after 6–8 weeks to ensure complete healing of the fistula. Recently covered SEMS with a large diameter and length have been introduced on the market, dedicated to the treatment of staple line leaks postlaparoscopic sleeve gastrectomy (Megastent, Taewoong Medical co, South Korea). It is a completely coated prosthesis with a large diameter (24–28 mm) and varying in length from 15 to 23 cm. This stent has two large flares in the proximal and distal part, ensuring an optimal gripping. Moreover, given its length, the proximal and distal ends can be opened upstream of the leak in the esophagus and in the duodenal bulb, respectively. This allows to reset the high pressure within the gastric tube, promoting the healing of the fistula. A recent case series by Galloro et al. showed that Megastent was effective in four patients with staple leaks, allowing rapid resumption of enteral nutrition and early discharge [26] (Fig. 5.3).

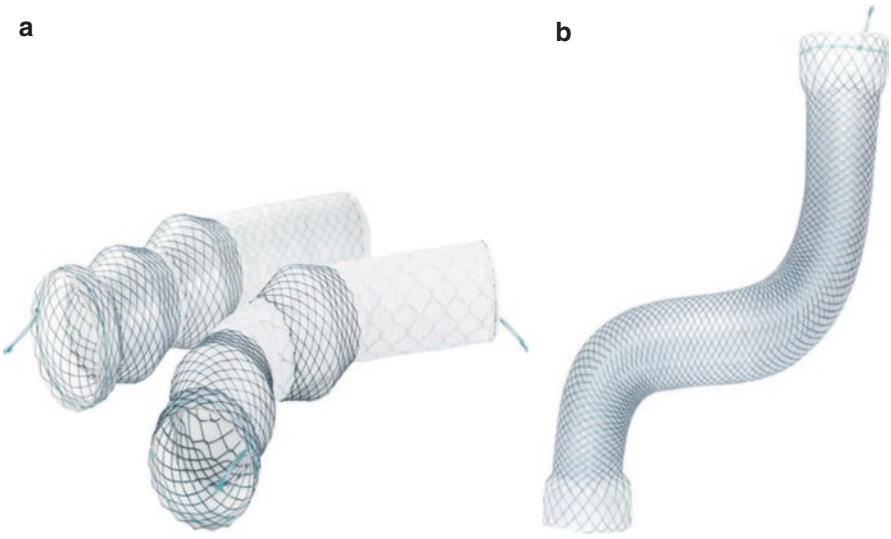

Fig. 5.3 Stent used to treat staple line leaks postlaparoscopic sleeve gastrectomy (**a** Betastent, Taewoong; **b** Megastent, Taewoong) (www.stent.net)

5.3 Unusual Application of Stents in Low GI Tract

Placement of SEMS within the low GI tract is an advanced endoscopic technique used to treat a variety of condition including obstruction, fistula, and perforation.

The most common indication for low GI tract stenting is the colon malignant obstruction. There are two major indications for colonic stenting in patients with colorectal cancer: palliation of advanced disease and preoperative decompression. In the latter case, placement of a stent can convert a surgical procedure from an emergent two-step procedure (including a colostomy) into an elective one-step resection with a primary anastomosis, which can be performed laparoscopically [29].

Large-bowel obstruction caused by advanced colon cancer occurs in three-fourths of all malignant colonic obstruction. The management of this severe clinical condition remains controversial.

The majority of colon cancer causing obstruction are localized to the left side of the colon, with the sigmoid colon being the most common location. Extrinsic colon cancer (in particular pelvic tumors) can infiltrate the colonic wall and may cause a lumen obstruction or a colonic compression. Malignant colonic obstruction may be treated by using conventional surgery with resection or diversion procedures, but patients presenting with malignant obstruction often are poor surgical candidates. Patients treated with a diverting colostomy frequently retain the stoma indefinitely because of the discovery of metastatic disease [30]. Urgent surgical intervention in this setting is associated with a mortality rate of 10 % and morbidity up to 40 % [31]. The most important endoscopic alternative to the urgent surgical management of malignant colonic obstruction is the placement of SEMS.

Over the last decade, many articles have been published on the subject of colonic stenting for malignant colonic obstruction, including randomized controlled trials (RCTs) and systematic reviews. However, the definitive role of self-expandable metal stents (SEMS) in the treatment of malignant colonic obstruction has not yet been clarified, and a collaborative approach to patient management, including surgeons and endoscopists, is recommended to guide patient care [31].

5.3.1 Self-Expanding Metallic Stents for Malignant Obstruction

Endoscopic placement of colorectal stents is an effective alternative to surgical decompression for colonic obstruction. In a pooled analysis of 54 trials, reporting on 1198 patients with malignant colorectal obstruction, SEMS placement achieved clinical success in 91 % [32]. In the most current review of 88 articles incorporating the results of SEMS placement in 1785 patients for malignant colonic obstruction, clinical success was achieved at a median rate of 92 % [33]. Serious complications, including colon perforations, were reported in 5 % of patients in each of these two papers.

Two precautions emerge from these studies. First, stricture dilation before or immediately after stent placement results in a five- to sixfold higher rate of perforation (10 %–18 %) and should generally be avoided [32]. Second, covered stents may have inferior outcomes compared with uncovered stents because of a significantly higher migration rate (31 % vs. 3 %) [33].

Although excellent right-side colonic SEMS placement outcomes have been reported from expert centers, data are more limited than for left-side colonic SEMS placement.

5.3.2 Colonic SEMS as a Bridge to Surgery

In patients with malignant colonic obstruction who are candidates for surgical resection, placement of a colonic SEMS allows colonic decompression without the morbidity and mortality of urgent surgery.

The most recent systematic review and meta-analysis evaluated the efficacy and safety of colonic stenting as a bridge to surgery ($n = 195$) compared with emergency surgery ($n = 187$). All seven RCTs that focused on the postoperative outcome of SEMS and emergency surgery were included in this meta-analysis. The mean technical success rate of colonic stent placement was 76.9 % (range 46.7 %–100 %). There was no statistically significant difference in the postoperative mortality comparing SEMS as bridge to surgery (10.7 %) and emergency surgery (12.4 %). The meta-analysis showed a lower overall morbidity (33.1 % vs. 53.9 %, $P = 0.03$), a higher successful primary anastomosis rate (67.2 % vs. 55.1 %, $P < 0.01$), and a lower permanent stoma rate (9 % vs. 27.4 %, $P < 0.01$) in the SEMS group [34].

According to these results, SEMS placement are related to significantly lower complication rates and shorter hospital stays, better health-related quality of life, and reduced costs.

Moreover, the relief of symptoms provided by SEMS placement allows additional time to stabilize the patient, address underlying comorbid medical illnesses, perform a thorough staging evaluation of the cancer, and offer the opportunity to provide neoadjuvant therapy in patients with rectal cancer. In this way, colorectal stent placement serves as a favorable "bridge to surgery." For those patients who appear to be surgical candidates but later are found to have widely metastatic disease, the SEMS can be left in place as palliative therapy and a potentially permanent colostomy avoided [35]

Oncological Outcomes Potential concerns have been found about impaired oncological results after SEMS treatment in the bridge to surgery group patient, particularly following colon stent perforation. The outcome of long-term follow-up comparing SEMS as a bridge to elective surgery versus acute resection was analyzed by three RCTs [36–38]. Although the study groups were small (15–26 patients in the stent arms), all trials report higher oncologic disease recurrence rates in the SEMS group. However, no difference in survival was seen in the SEMS group compared with the surgery group in the three trials [36–38].

The use of SEMS and the occurrence of tumor stenting perforation were identified to correlate with worse overall survival. The outcome data of the "Dutch Stent-In 2" trial showed a significantly higher overall recurrence disease rate in the SEMS group between the two arms (42 % in the surgical group vs. 25 % in the SEMS group), which was even higher in the subgroup of patients who experienced stent-related perforation (83 %) [38]. The oncological risks of SEMS placement should be balanced against the operative risks of emergency surgery. Because there is no reduction in postoperative mortality and stenting seems to impact on the oncological safety, the use of SEMS as a bridge to surgery could not be recommended as a standard treatment for potentially curable patients. However, placement of SEMS is considered an alternative option in patients at high surgical risk.

Risk factors as increasing age and an ASA score ≥ III are associated with adverse outcomes following elective as well as emergency surgery in colorectal cancer. Therefore, the use of SEMS as a bridge to elective surgery may be considered the preferred alternative treatment option in patients potentially unfit for surgery: older than 70 years and/or with an ASA score ≥ III [39].

5.3.3 Colonic SEMS as Palliative Therapy

Colonic SEMS can also provide effective palliation for patients with malignant colonic obstruction who are recognized at initial evaluation to be poor operative candidates. Follow-up data of colonic SEMS placement for palliation are favorable; the median rate of clinical success was 90 %–93 %, and the median rate of

reobstruction ranges from 12 % to 16 % [32, 33] Patients who underwent to colonic SEMS placement as palliative therapy, compared with surgery, had lower medical complications, shorter hospitalization, reduced number of colostomy [40, 41], more prompt initiation of chemotherapy [42], and a trend toward decreased mortality [43].

In recognition of these findings, recent reviews support endoscopic placement of colonic SEMS as an effective approach to palliation of patients with stage IV colon cancer obstruction.

Colonic SEMS also may serve for palliation of rectal cancer. Hünerbein et al. achieved initial technical success in 33 out of 34 patients (97 %) but suggested that stent placement is contraindicated for low rectal cancer (5 cm from anal verge) because of tenesmus and patient's incontinence [44].

According to the results of two meta-analyses [45, 46], colon SEMS are related to a significant lower 30-day mortality (4% vs. 11 %, SEMS vs. surgery, respectively), a shorter hospitalization (10 vs. 19 days), and a lower intensive care unit (ICU) admission (0.8 % vs. 18.0 %) while permitting a shorter time to initiation of chemotherapy (16 vs. 33 days). Surgical stoma formation was significantly lower after palliative SEMS compared with emergency surgery (13 % vs. 54 %).

No significant difference in overall morbidity between the stent group (34 %) and the surgery group (38 %) has been observed. Early complications did occur more often in the surgery group, while higher late complications were more frequent in the SEMS group. The most frequent stent-related complications in the SEMS palliative group included colon perforation (10 %), stent migration (9 %), and reobstruction (18 %) [45, 46].

Together, these analyses demonstrate that SEMS placement provides cost-effective relief of malignant colonic obstruction with an acceptable rate of complications in a broad population of patients.

Chemotherapy without anti-angiogenic agents (bevacizumab) is not associated with an increased risk of colon stent perforation. Patients who have undergone palliative stenting can be safely treated with chemotherapy without anti-angiogenic agents [47].

Retrospective series found an increased risk of stent-related colon perforation (17–50 %) in patients treated with angiogenesis inhibitor [48]. A meta-analysis found the treatment with anti-angiogenic agents as a risk factor of increased colon perforation during colon stenting: 12.5 % of colon perforation rate was observed in patients treated with bevacizumab compared to 7.0 % of colon perforation registered in patients treated with standard chemotherapy [47]. Considered the high risk of colon perforation identified in this subgroup of patient, the use of SEMS as palliative treatment is not recommended if an anti-angiogenic therapy is being administered [47].

5.3.4 SEMS in Benign Colorectal Diseases

There are two major applications of SEMS in this field: benign colorectal obstruction and colorectal fistula.

Colorectal obstruction could be associated to diverticulitis, post-actinc stricture, IBD-related stricture, postsurgical anastomotic stricture. Management of benign colorectal obstructive disease is a challenging effort. Endoscopic balloon dilation is the most used and simplest therapeutic choice, but it is associated with a high recurrence rate, and refractoriness is observed in more than 20 % of cases [49]. Results concerning the long-term obstruction symptom relief in patients with benign colon obstructive disease have been obtained in heterogeneous series, and there is some controversy about efficacy and safety [50–54]. Stents have not been so commonly studied in patients with benign colorectal obstruction. Few and controversial data are available on the application of SEMS in Crohn's disease (CD) strictures. Clinical success ranges from 45 % to 80 % in published series involving patients with postsurgical strictures mostly [55]. Loras et al. found an overall efficacy of 64.7 % after a follow-up of 60 weeks. Patient's refractory to balloon endoscopic treatment or cases in which balloon dilations were unsuitable have been included in this series. The results showed that this technique may offer an alternative to endoscopic treatment considered the limited minor complications (distal migration in 52 % of cases). Authors conclude that placement of FCSEMS in CD strictures maintained over a period of 4 weeks is a safe and effective treatment for strictures refractory to endoscopic dilatations; the length and location of stricture are important considerations for the correct choice of the stent [55].

Keranen et al.'s series included patients with diverticular colon obstruction (n = 10) remarking a high major complication rate with colon perforation observed in three out of ten patients. High colon perforation rates were found in other series in which diverticular strictures were treated with SEMS: Small AJ et al. noted two cases of colon perforation out of 14 patients treated with SEMS [51, 55].

The application of SEMS in diverticular disease is complicated by high perforation rate in both palliative and bridge to surgery cases. This may be due to persisting sepsis or inflammatory activity making the bowel friable and susceptible to local damage. According to these results, the use of SEMS for obstruction caused by diverticulitis has not been recommended because of concern for high perforation rate.

The best results on the applications of FCSEMS in benign colorectal strictures have been reached in colorectal anastomotic stenosis. Caruso et al. showed an early clinical success in the absence of endoscopic or surgical reintervention in all cases. Prolonged clinical success (median follow-up of 21 months) was reached in 56 % cases. Complications consisted of spontaneous stent migration only and occurred in 19 % of cases. The multivariate analysis of this retrospective series showed a lower stent migration rate (19 %) when large-diameter stents (i.e., 24–26 mm) were used, in turn favoring clinical success. According to these data, FCSEMS can represent effective and safe treatment for anastomotic colorectal strictures, and large stents are warranted for better results [56]. Similarly, Vanbiervliet et al. [57] found a recurrence rate in half (53 %) of patients treated with SEMS for postsurgical colon stricture obstruction in long-term follow-up and high stent migration rate (63 %) occurred.

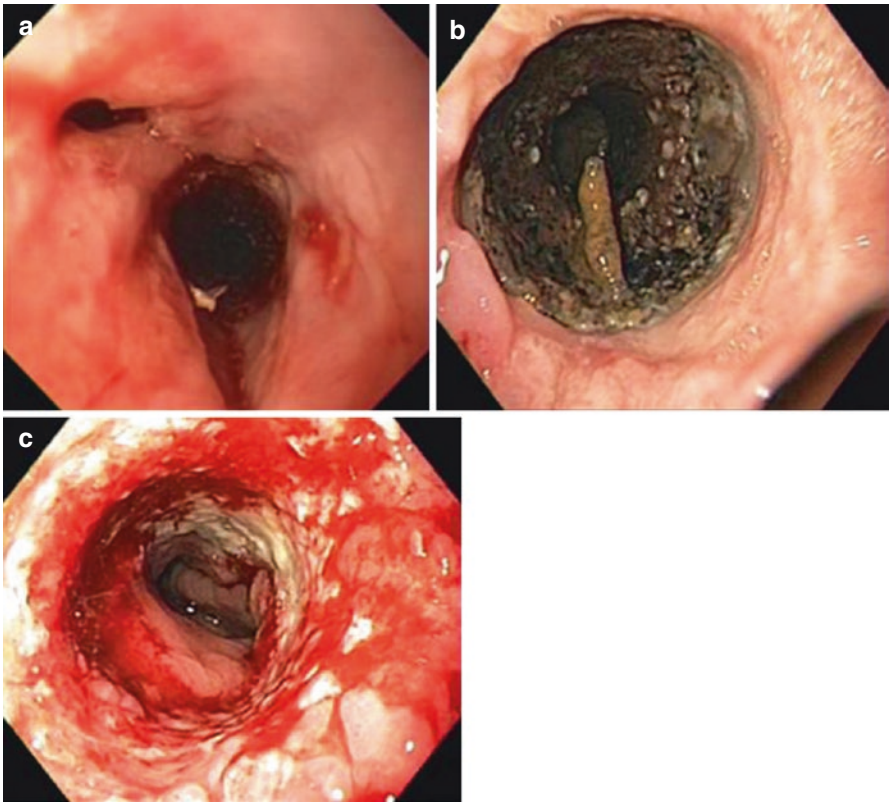

Fig. 5.4 Example of fistula closure using SEMS. (**a**) Fistula across a colorectal anastomotic rhyme. (**b**) FCSEMS has been positioned across the anastomosis. (**c**) Fistula healing after stent retrieval

In small case series, SEMS have been applied as nonsurgical therapeutic option to heal a colorectal fistula [51, 58]. Mostly data deal with the use of SEMS in anastomotic leak (Figs. 5.4 and 5.5). Authors have used both covered and uncovered SEMS registering the absence of migration in all cases and an overall long-term clinical efficacy of 73 %.

In our center, few cases with good results have been treated using biodegradable stents in alternative to FCSEMS when a postsurgical fistula is associated to the anastomotic stricture; in this pattern, biodegradable stent helps to heal fistula, thanks to the overgrowth tissue stimulation, and stenosis should be treated, thanks to the intrinsic high radial force of biodegradable stent (Fig. 5.6).

Likewise biodegradable stents, uncovered stents induce hyperplastic and overgrowth tissue reaction permitting fistula closure, but uncovered stents are very difficult to be removed endoscopically. FCSEMS can be safely removed endoscopically but are complicated by migration in 30 %–60 % of cases.

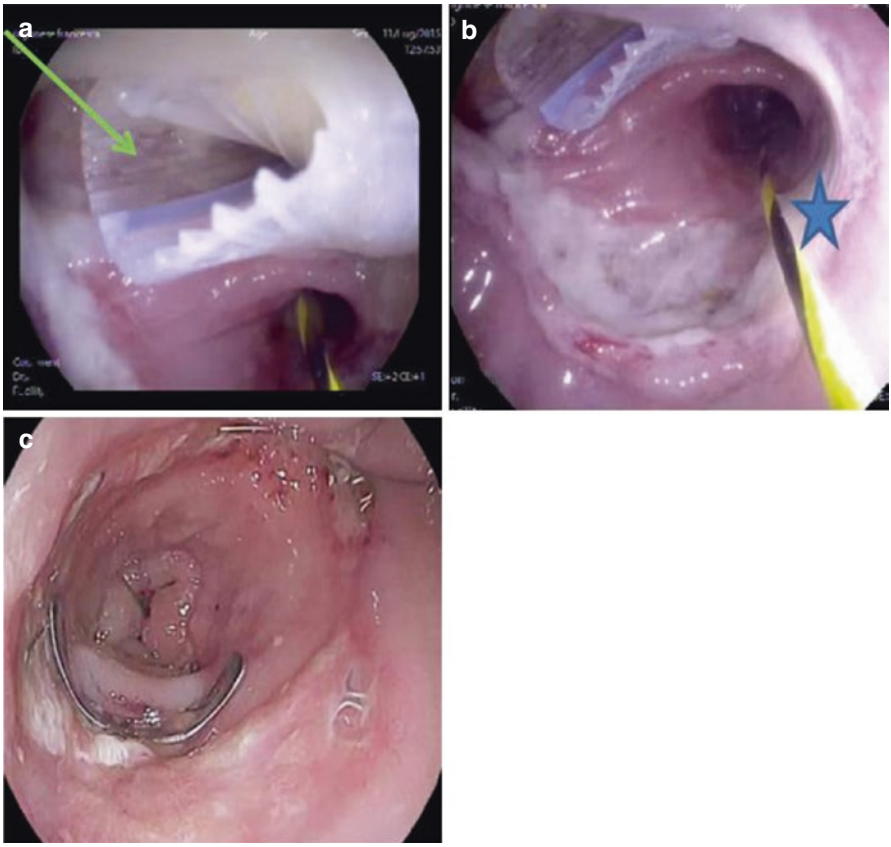

Fig. 5.5 Postsurgical colon dehiscence. (**a**) Penrose tube drainage (*arrow*) is located through the anastomotic dehiscence in the colon lumen. (**b**) Through a guidewire (*star*), a colon SEMS is placed across the anastomosis. (**c**) Anastomotic healing after 6 months of follow-up: an OTSC (over-the-scope clip) has been released in the site of dehiscence at the same time of stent placement to improve the possibility of anastomotic healing

The absence of migration in the series cited above [58] is uncommon, and the long-term management of patients treated with SEMS concerning the undefined long-time uncovered stent placement is unclear.

Covered SEMS have several potential advantages over uncovered or plastic stents.

The overgrowth of mucosal hyperplastic reaction in uncovered and partially covered SEMS facilitate the impaction of the stent with difficulties in removal; therefore, these types of stents are less ideal for the treatment of benign strictures [55]. Owing to their flexibility, FCSEMS are easier to insert and deploy, and retrieval is easier owing to absent overgrowth tissue.

Experiences from different centers with a larger number of patients are needed, before any definitive conclusion or clinical application can be accepted.

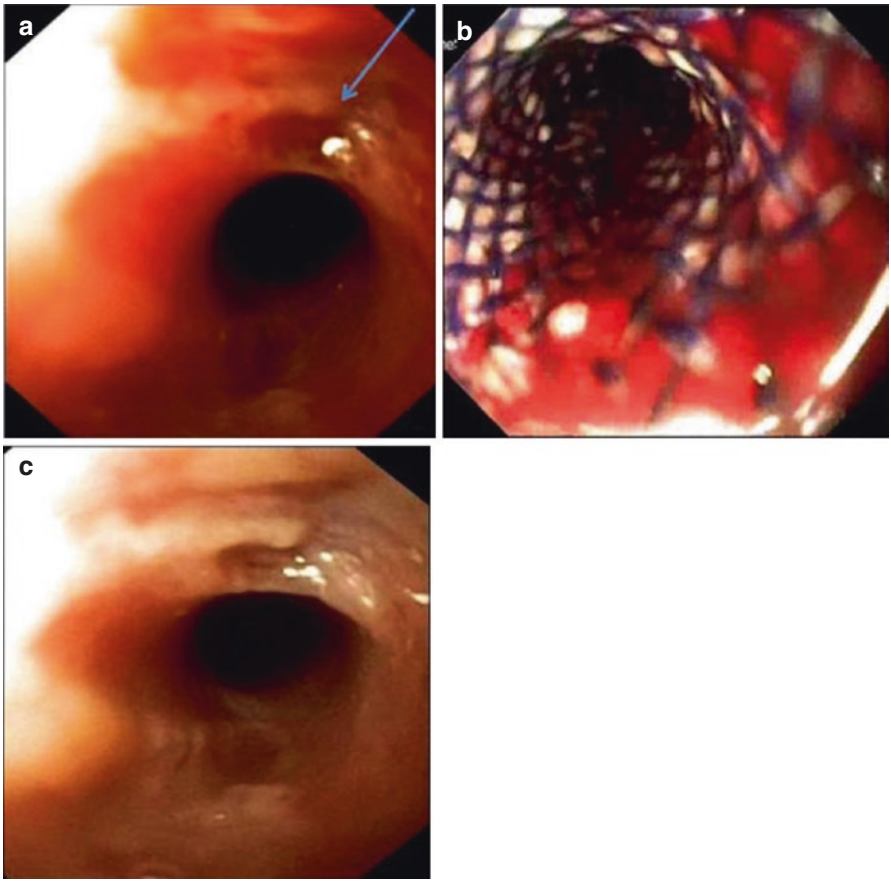

Fig. 5.6 Biodegradable stent applied in anastomotic postsurgical stricture associated to fistula: (**a**) *Arrow* shows fistula in the colon anastomotic stricture. (**b**) Biodegradable stent is released. (**c**) Results after 5 months of follow-up: fistula is closed and anastomotic colon orifice has a larger diameter

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