



Endoscopic stenting in colorectal cancer

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Abstract: Acute malignant large bowel obstruction presents as one of the few emergencies of colorectal cancer (CRC). Management of this condition can either be by (I) upfront surgery or (II) the use of self-expanding metallic stent (SEMS) as a bridge to elective surgery. For patients with metastasis, the use of SEMS is reported to enable earlier commencement of chemotherapy. Although the use of SEMS in patients with acute malignant large bowel obstruction looks promising, it is plagued by its own set of complications and divided opinion over its long-term outcomes. Conflicting data are present, and definitive indication requires further evaluation and debate. This article will describe the typical presentation of patients with acute malignant large bowel obstruction. An introduction to the SEMS insertion procedural steps will be undertaken. Following which the article aims to review the safety profile of SEMS and the short- and long-term outcomes of SEMS in both the curative and palliative setting.

Keywords: Colorectal cancer (CRC); obstruction; stenting; self-expanding metallic stent (SEMS)

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Introduction

Colorectal cancer (CRC) is one of the most common cancer in the world (1). Large bowel obstruction is one of the few emergency presentations of CRC. Studies have showed that the proportion of CRC patients admitted to hospital as an acute emergency case hover around 10–30% for the past 5 years (2–4).

Emergency surgery for acute malignant large bowel obstruction is associated with morbidity rates of 40–60% and mortality of 3–11% (5–7). Peri-operative complications such as death, sepsis, anastomotic leaks, wound infection and cerebrovascular accidents are usually encountered, with the addition of higher rates of permanent stoma formation (8).

The use of self-expanding metallic stents (SEMS) was first described for the management of acute large bowel obstruction since the early 1990s by Tejero *et al.* (9). The use of SEMS has progressed from palliating advanced CRC

and as a means to bridge the need for emergent surgery to an elective one (10).

Since then, the short- and long-term outcomes of endoscopic colonic stenting have been reviewed with its safety profile being determined to minimize any potential harm to any patient receiving this form of treatment. For patients with acute large bowel obstruction presenting with metastatic disease, we have to evaluate the role endoscopic colonic stenting play in palliating the obstruction. Numerous randomized controlled trials were conducted comparing the use of SEMS as a bridge to surgery versus emergency surgery for the management of acute malignant large bowel obstruction (11–17). The rationale for such a move is to provide swift and effective decompression of the large bowel, minimize the risk of bacterial translocation, whilst allowing for proper oncological staging, physiological optimization and resuscitation before having the patient undergo surgery in an elective setting.

Numerous studies have been performed to evaluate the role of SEMS in malignant large bowel obstruction, however several of them highlighted contrasting results. Hence, we conducted this review article to evaluate the evidence of the role of SEMS in the management of patients with acute malignant large bowel obstruction.

Patient selection

The management of patients presenting with acute malignant left-sided large bowel obstruction, including the rectum should be individualized. Proper patient selection is crucial in ensuring good outcome. The group of patients who may be affected by this condition are usually older and hence a comprehensive review of their medical comorbidities is of particular importance to determine their fitness for surgery (7). Studies have reported that almost 70–80% of large bowel obstruction are actually located in the left side of the colon, which makes them amenable to endoscopic interventions (18,19). Of which about 10% of these patients will require emergency surgery and are associated with poor outcomes with morbidity as high as 70% and mortality reaching 12% (7,20). Compared to the morbidity levels of elective surgery for CRC which are reported to be less than 5% (21).

Options for treatment may include staged surgical resection with or without anastomosis (e.g., Hartmann resection), resection of the distended bowel (e.g., subtotal/total colectomy), or temporary relief of obstruction and faecal load (e.g., creation of proximal defunctioning loop colostomy or ileostomy or the use of endoscopic stenting through the stenosed segment as a bridge to surgery in an elective setting). A tumour in the lower rectum cannot be stented as the distal end of the stent will cause tenesmus and faecal incontinence giving rise to poorer quality of life (22). We need to consider the patient factor, disease factor through CT scan (site of obstruction, length of stenosis, presence of metastasis, perforation) and available expertise, which will be further elaborated in this review. Each of these options has advantages and disadvantages and the ultimate decision must be made with the best interest of the patient and the clinical presentation in mind (23).

Overview of self-expanding metallic stents

There are no large-scale studies to determine the superiority of the SEMS that are currently in the market. Variables such as material, design, diameter, length,

flexibility, foreshortening ratio and delivery system are considered when selecting appropriate SEMS for each individual patient (23–27).

There are many endoscopic colonic stents available in the market. Majority of the stents are made of nitinol (alloy of nickel and titanium) which enables good flexibility and elasticity allowing for smooth deployment (28,29). Examples of which are Ultraflex (Boston Scientific, Natick, MA, USA) and Alimaxx E (Alveolus, Charlotte, NC, USA) stents. Other materials include stainless steel (i.e., Z-stent) (Cook Medical, Bloomington, IN, USA) and Elgiloy (alloy of cobalt, chromium and nickel) (i.e., Wallstent) (Boston Scientific, Natick, MA, USA) (29). Colonic stents can be broadly divided into two main groups: uncovered and covered. Recent meta-analysis comparing the technical success rates of these two groups showed no significant difference (29). The studies also reported similar stent migration rates (30,31). However, the benefit conferred by inserting a covered colonic stent is the association with higher tumour in-growth (RR 6; 95% CI: 2.23–16.1, $P=0.0004$) (30,32). This is an important aspect to consider when performing palliative endoscopic colonic stenting, in order to avoid having to go through another intervention subsequently.

Description of the endoscopic colonic stenting procedure using SEMS

The procedure is carried out endoscopically under image intensifier guidance at the endoscopy suite, the fluoroscopy room at the department of diagnostics imaging using portable endoscopic equipment, or the operating theatre (especially if there is a hybrid theatre for endovascular procedures). Access to an operating facility is required as abdominal distention secondary to gas insufflation during the stenting procedure can lead to inadvertent perforation, necessitating immediate transfer to the operating theatre (33).

When possible, ensure that the patient receives a rectal enema for clearance of the bowel distal to the obstruction before stenting to facilitate scope insertion (34). Prior to the procedure, the patient is positioned in the left lateral position under conscious sedation. A double lumen colonoscope is preferred as it facilitates simultaneous suction and irrigation via one channel whilst advancing the guidewire in the other channel. If available, carbon dioxide insufflation should be used in preference to room air.

The distal end of the stenosing malignant lesion will be encountered (*Figure 1*). Identify any area on the tumour



Figure 1 Endoscopic view of the distal end of stenotic lesion.



Figure 2 Fluoroscopic delineation of stenotic lesion.

that will allow passage of the lipophilic guidewire into the proximal bowel, and advance the guidewire under fluoroscopy (*Figure 2*). Multiple attempts of passing the guidewire may be necessary. The cannula is then inserted over the guidewire using the Seldinger technique into the proximal bowel to allow injection of water soluble radiological contrast to establish the proximal and distal extent of the tumour using fluoroscopy (*Figure 3*). The length of the tumour is measured before deciding on the optimal length of stent to be used. There needs to be sufficient stent overhang on both ends of the tumour to minimize migration of the stent after full expansion.

The cannula is then exchanged for the stent in its deploying device, whilst keeping the guidewire in its original position. Frequent confirmation with fluoroscopy during

this step is required. The stent deploying device is advanced under direct fluoroscopy and endoscopic visualization until the entire stent is deployed. There is a need for counter-traction on the device during the deployment phase as there is a tendency for the stent to be drawn into the proximal bowel due to the radial expansion of the stent (*Figure 4*) (35). Simultaneous monitoring with fluoroscopy and direct vision via endoscopy is mandatory (*Figure 5*). Once the stent is fully deployed successfully (*Figure 6*), its position is confirmed under fluoroscopy. The distal end of the stent should be visible beyond the malignant lesion, and a gush of faeculent material should be encountered (*Figure 7*).

The patient is usually monitored overnight and an abdominal X-ray is taken within the next 24 hours to confirm the position and expansion of the stent. A vigilant look out for immediate post-procedural complications such as perforation is required. Oral intake can resume once the abdominal distension resolves. The patient is routinely prescribed stool softeners and a low residue diet, to enable ease of passage of stools. Most colonic stents expand to a diameter of 25 mm as described above, hence high dietary fibre can theoretically cause obstruction of the stent (32).

Short-term outcomes of the use of SEMS in endoscopic colonic stenting

There are numerous randomized controlled trials and systematic reviews that have compared endoscopic colonic stenting versus emergency surgery for acute malignant left-sided large bowel obstruction (4,5,8,10,35). Endoscopic colonic stenting has been recognized as a safe and effective means to alleviate acute large bowel obstruction and act as a bridge to curative surgery performed in an elective setting. The role of pre-operative stenting in the emergent management of acute malignant large bowel obstruction has been supportive by several pooled analyses that demonstrate efficacy and safety and cost-effectiveness analysis studies as described (36,37).

Predictors for failed SEMS deployment

There are some technical considerations that the endoscopist should note before undertaking the procedure to achieve a successful stent deployment. Technical failure can be defined in the following scenarios: (I) inability to cannulate the guide wire through the tumour, and (II) unsuccessful stent deployment. Clinical failure occurs when there is a failure of the deployed stent to relieve the

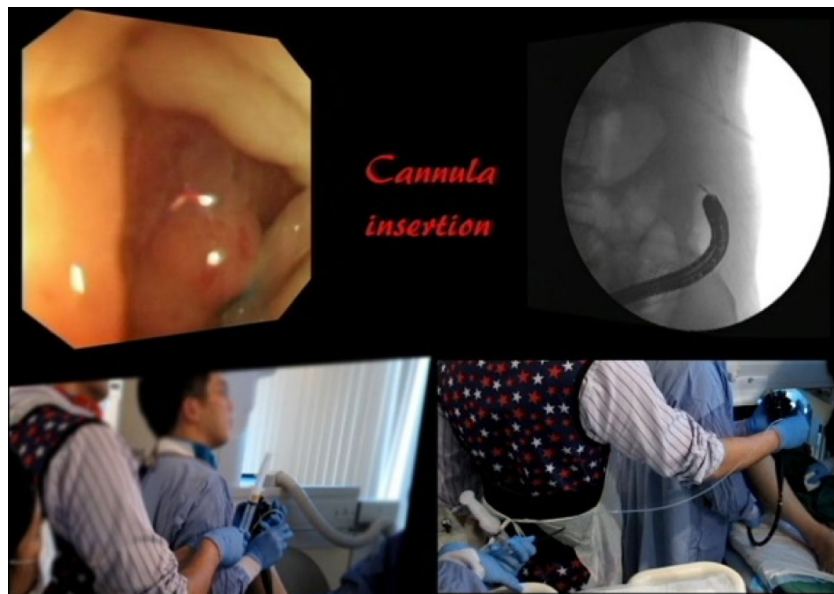


Figure 3 Cannula insertion over guidewire using Seldinger technique.



Figure 4 The need for counter-traction during the SEMS deployment phase. SEMS, self-expanding metallic stent.



Figure 5 Full deployment of SEMS under endoscopic and fluoroscopic views. SEMS, self-expanding metallic stent.

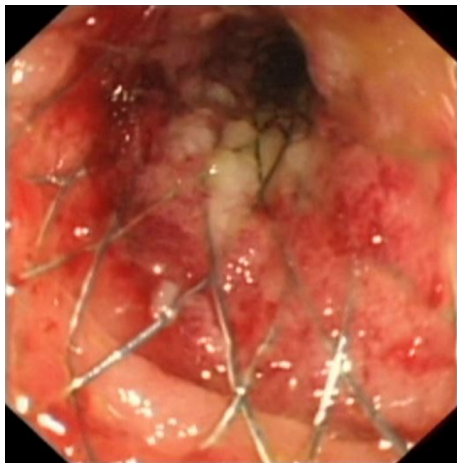


Figure 6 Stented malignant lesion.

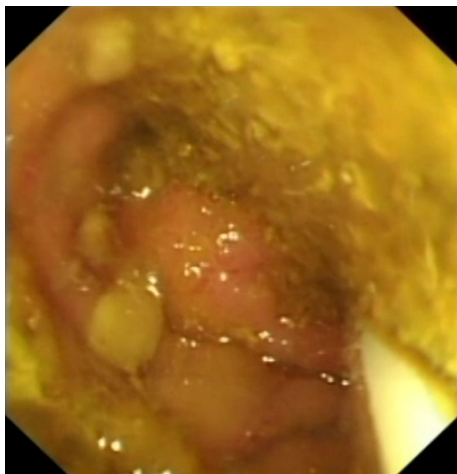


Figure 7 Gush of faeculent material upon successful deployment of SEMS. SEMS, self-expanding metallic stent.

obstruction, often due to inadequate expansion requiring subsequent surgical decompression. It is reported in systemic reviews that the technical success rates range from 80–90%, while the clinical success rates hovers around 70–80% (38). Little *et al.* observed that technical success rates decreased when the onset of symptoms is more than 1 week resulting in a drop from 85.4% to 69.6% (39).

Patients who failed endoscopic colonic stenting and had to undergo subsequent emergent surgery are 3 times (OR 3.3; 95% CI: 1.19–9.20; $P=0.026$) more likely to experience worse outcomes compared to those who had emergency surgery upfront (40). To avoid such morbidities, the suitability for stenting has to be evaluated on CT scan

including anatomical considerations (e.g., tumour location and length of the stricture) and availability of adequate expertise.

Firstly, an evaluation of the length of stenosis has to be performed. Failures are more frequently encountered in cases where the stenosis is longer than 4 cm due to inadequate stent expansion (34,39). The recommended stent length should be sufficient to bridge the stenosed segment and provide an overhang of at least 2 cm on each side of the malignant lesion (19,41). What is promising is the use of multiple stents to bridge a long segment of obstruction or the presence of synchronous lesions by a few case reports to overcome this issue (28).

Next, the angulation of the lumen present at the area of malignant stenosis. Acute angulations of more than 165 degrees between the malignant lesion and distal lumen is associated with higher failure rates (40). Such acute angulations are postulated to be due to invasion of the underlying structures, making the stenting procedure more challenging and occasionally impossible (39). Thirdly, the degree of stenosis of the malignant lesion. It is reported that the risk of bowel perforation increases by 7 times (OR 6.88; 95% CI: 2.0–23.2, $P=0.002$) in the presence of complete large bowel obstruction compared to those with sub-total obstruction (42). CT imaging may reveal the presence of caecal pneumatosis for patients with acute large bowel obstruction. A review has shown that not all caecal pneumatosis is associated with non-viable caecum and its presence does not pose as an absolute contra-indication to endoscopic stenting (43).

Next, extra-colonic origin of large bowel obstruction can disrupt the colonic luminal patency (44). Overall technical success for the use of SEMS in these instances range from 42% to 100% and clinical success rates of 25–87.5% (45–50). Despite these success rates, it is observed that the luminal patency is lower in those with extra-colonic malignancies compared to those with intrinsic malignancies (51).

Lastly, there is a steep learning curve for the proceduralist performing the stenting procedure. Its availability depends on local expertise and the availability of fluoroscopy, as well as the specialized endoscopic equipment for the stent placement. The level of expertise present in the institution has a direct correlation to the rates of successful stenting and complications (52,53). To increase the chances for success, the proceduralist is expected to have attempted more than 20 procedures and be familiar with other endoscopic procedures like the endoscopic retrograde cholangiopancreatography (ERCP) (54,55).

Outcomes of successful SEMS deployment

Outcomes such as clinical success rates, peri-operative outcomes and rates of primary anastomosis are commonly reviewed. In a comparison between endoscopic colonic stenting and emergency surgery, the stenting procedure confers superior clinical success rates (98.6% *vs.* 78.1%) with similar post intervention outcomes (56). Thirty-day mortality (2.3%) was reported to be low, with similar overall complication rates [33.1–39.2% (stent) *vs.* 45.7–53.9% (emergency surgery)] in both groups (56,57). The preferable outcomes led to shorter length of hospital stay in the stenting group (6 *vs.* 8 days, $P=0.028$) (15), making it a more cost-effective option than emergency surgery during the initial hospitalization stay (18).

During the subsequent elective surgery, laparoscopic approach can be attempted to reap benefits such as lower rates of ileus, lesser pain, shorter duration of analgesia use, and length of hospital stay (58). Large bowel obstruction used to be considered as a relative contraindication to laparoscopic approach given the poor surgical field that could be encountered due to the presence of distended bowel and likelihood of bowel injury (59). However, the use of SEMS can improve the eventual surgical field by decompressing the distended bowel and reducing the degree of bowel oedema prior to the elective surgery which facilitates primary anastomosis (60).

Studies have reported higher primary anastomosis rates (RR 1.58; 95% CI: 1.22–2.04, $P<0.001$) (57). However, in a systematic review and meta-analysis performed by Cirocchi *et al.*, there was no difference in primary anastomosis rates between the stenting and surgery group (37). But the non-randomised studies seem to suggest that endoscopic colonic stenting facilitates the occurrence of one-stage surgical intervention (67.2% *vs.* 55.1%, $P<0.01$) (34,57), with success rates for single stage elective surgery to be 60–85% (53,61). There was no significant difference between the two groups regarding anastomotic leakage (4.1% *vs.* 5.9%) (OR 0.74; 95% CI: 0.33–1.67, $P=0.47$) and intra-abdominal infection (1.4% *vs.* 3.2%) (OR 0.62; 95% CI: 0.12–3.19, $P=0.57$) (62,63).

In a meta-analysis that was performed by Allievi *et al.*, endoscopic colonic stenting as a bridge to surgery appears to be a safe approach with advantages such as reducing the incidence of peri-operative complication rates (37.8% *vs.* 54.9%) and lower stoma rates (28.8% *vs.* 46%), with no difference in overall mortality rates (10%) (57,62,64). This was concurred by Arezzo *et al.* who reported in meta-

analysis that the use of SEMS as a bridge to elective surgery is associated with lower overall morbidity (33.9% *vs.* 51.2%, $P=0.03$) and rates of temporary (33.9% *vs.* 51.4%) (65) and permanent (9% *vs.* 27.4%, $P<0.01$) stoma creation (34).

Stent-related complications

Complications arising from the insertion of SEMS can be divided by the degree of severity (minor or major), and early (≤ 30 days) or late (>30 days). The risk of endoscopic colonic stenting will have to be discussed with the patient prior to the procedure. It is advisable to obtain consent of the patient for possible surgical intervention in the event that the stenting is not successful. Major complications such as stent perforation (4–8%), migration (3–10%), and re-obstruction from tumour in-growth (3–10%) have to be explained (9,39,57), while minor complications include bleeding, pain, tenesmus and incontinence described (10,36).

Major complication—perforation

Initial clinical trials performed by the Dutch raised concerns over the safety of endoscopic colonic stenting, which led to early termination of the trial given high perforation and anastomotic leak rates (17). Postulation for the high perforation rates was associated with balloon pre-dilation; something my institution does not practice (66). We have to be mindful that despite reports of clinical perforation rates hovering around 7% but a histological analysis of surgical specimens revealed higher perforation rates of up to 14% (62). Increased risk of perforation is observed when anti-angiogenic agents like bevacizumab is used (9). However, recent studies have recognized colonic stenting as an accepted treatment approach for obstructing left sided colonic malignancy particularly as a bridge to palliative therapy (64). Stent related perforation can occur immediately or delayed. Immediate causes of perforation include wire or catheter misplacement. While, predictors for delayed perforation include the presence of thin-walled caecum, placement of SEMS at the recto-sigmoid junction with sharp angulation and excessive amount of air insufflation in a distended large bowel (28,67,68).

Major complication—stent migration and re-obstruction

Stent migration rates of covered stents (8–50%) exceeds uncovered stents (3–36%) (69). This occurs when the stent diameter is too narrow or too short in length in comparison

with the obstructing segment, or if the lesion shrinks after chemotherapy (70). Stent re-obstruction occurs over time if the cancer is not removed. Treatment options include surgery or repeated stenting (71). New strategies will have to be in place to avoid stent-related complications and prolong stent patency (35). With the development of new material and design, or the presence of drug eluting stents, we can reduce the chance of developing stent migration and re-obstruction. In one animal study that validated the usefulness of 5-fluorouracil-loaded polydioxanone stent for the treatment of CRC, in-stent re-stenosis was reduced by 50% (6.4% vs. 12.8%) (72).

Minor complications

Bleeding can usually be treated conservatively, with pain relief provided through the use of analgesia. Faecal incontinence can be avoided if the SEMS is placed at least 2 cm proximal to anal verge (68).

Long-term outcomes of the use of SEMS in endoscopic colonic stenting

The literature is still divided regarding the long-term outcomes of endoscopic colonic stenting. There were three studies from the west which reported lower overall survival rates for patients who underwent endoscopic colonic stenting with a higher 5-year cancer specific mortality (48% vs. 21%) (73). On the other hand, other studies showed no difference in overall survival (97.8% vs. 94.3%, $P=0.469$) and 5-year disease free survival (79.6% vs. 70.2%, $P=0.218$) given similar uptake of adjuvant chemotherapy and lymph node harvested (74,75).

In a prospective cohort study by Gorissen *et al.* it showed higher local recurrence rates (32% vs. 8%, $P=0.027$) in patients who received endoscopic colonic stenting (74). A postulation for observed increased in local recurrence rates (73) is the presence of higher rates of peri-neural invasion in the histopathological assessment of the stented colonic segments (4). The pressure effect exerted by the SEMS could potentially have induced tumour cell invasion into the nerves via the dissemination of cancer cells during the procedure (76). A predictor for higher loco-regional recurrence and distant metastasis rates was also associated with the presence of stent related perforation as observed in a study by Sloothaak *et al.* (83% stent with perforation vs. 28% surgery only vs. 40% stent without perforation). This lead to worse disease free survival rates in the subgroup with

stent related perforation (0% vs. 45%, $P=0.007$) (77).

The prognostic impact of endoscopic colonic stenting remains unclear (57,74,78), further studies will be required to determine its impact on overall survival and disease free survival in this population (11,13,77,79). Current literature seem to suggest that SEMS is a good treatment option to palliate patients with obstructed colonic anastomosis sites due to cancer recurrences (29).

Outcomes of patients receiving treatment for palliative intent

Endoscopic colonic stenting using SEMS represents an alternative to colostomy for patients with inoperable malignant colonic lesions presenting with large bowel obstruction (80). The European Society of Gastrointestinal Endoscopy (ESGE) recommends that endoscopic colonic stenting using SEMS is the preferred treatment for palliation of malignant large bowel obstruction (34). Two systematic reviews were performed comparing palliative endoscopic colonic stenting versus emergent surgery (81,82). The benefits of endoscopic colonic stenting performed in patients with metastatic large bowel obstruction include shorter hospital stay (5 vs. 12 days, $P=0.003$), earlier initiation of chemotherapy (4 vs. 7 weeks, $P=0.02$), and lower stoma formation rates (OR 0.19; 95% CI: 0.12–0.28), $P<0.01$) (82,83).

Patients should also be counselled on the possible stent related complications that can occur, such as perforation (8–10%), migration (8.4–9.2%) and re-obstruction (13.1–18.3%) (83). Patients managed with palliative endoscopic colonic stenting can be treated safely with chemotherapy without anti-angiogenic agents as recommended by ESGE (34). This is because several retrospective studies have showed an increase risk of perforation when bevacizumab is used (84,85).

The importance of chemotherapy after surgery in metastatic CRC cannot be understated (86–90). Although the stenting procedure itself does not confer any survival benefit (7.6 vs. 7.8 months) (82), it increases the possibility of down-staging previously unresectable metastatic disease (91). To allow these patients the chance to have better long-term outcome, the ability to administer chemotherapy within a certain therapeutic window is important, beyond which, the benefits are questionable as the role of palliative endoscopic colonic stenting in patients who have resectable metastasis is unclear (92). What is crucial for these patients is the earlier commencement of

chemotherapy which has been shown to increase survival from 9 to 24 months and the potential to downstage the disease (93,94).

Numerous studies have confirmed the significant improvement in the quality of life in stage IV CRC patients who were successfully stented for their malignant obstruction. A randomized controlled trial performed by Young *et al.* showed that patients stenting in patients with obstructed stage IV disease was associated with better quality of life outcomes when compared to baseline at 1 week (58% *vs.* 27%), and at 12 months ($P=0.001$ and $P=0.01$), without worse clinical outcomes in terms of 30-day mortality and median overall survival (95). This concurs with non-randomised studies which have shown improved overall quality of life, as well as life relating to gastrointestinal symptoms in patients who underwent stenting instead of emergency surgical decompression (96).

Way ahead

The indication of SEMs can be expanded to include benign conditions but this remains debatable for there is a need to reconcile the risk of stent related complications (97). In the management of benign strictures, the use of biodegradable stents have been attempted. The case series from the Czech Republic included three patients with Crohn's disease where balloon dilatation of the stenosis followed by biodegradable stent placement showed favorable results (i.e., degradable of stent within 4 months), with no stent migration or major complications (98).

In addition, alternative management of anastomotic leaks after colorectal surgery, is the novel use of covered SEMs. Reports of success rates ranging from 53.3% to 73.3% have been seen (99). However, increased risk of stent migration (up to 40%) given the used of covered SEMs will have to be undertaken.

Conclusions

Benefits of the use of SEMs as a bridge to surgery should be compared with the potential risk of complications arising from endoscopic colonic stenting. Given ongoing review of its long-term outcomes (i.e., local recurrence and metastatic spread) and safety profile (i.e., stent related adverse events), the official statement from the ESGE and the American Society for Gastrointestinal Endoscopy (ASGE) recommends that (I) the use of colonic SEMs as a bridge to elective surgery is not the standard treatment of

symptomatic left-sided malignant colonic obstruction and (II) SEMs placement may be considered as an alternative to emergency surgery in those who have increased risk of post-operative mortality [i.e., American Society of Anaesthesiologists (ASA) Physical Status \geq III and/or >70 years old (34,73)]. Conflicting data are present, and definitive indication requires further evaluation and debate.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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