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Acute left-sided malignant colonic obstruction: Is there a role for endoscopic stenting?

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Abstract

One of the biggest challenges in clinical practice remains the management of left-sided malignant colonic obstruction. Numerous studies on colonic stenting for neoplastic colonic obstruction have been reported in the last decades. Thereby the role of self-expandable metal stents (SEMS) in the treatment of malignant colonic obstruction has become better defined. However, numerous prospective and retrospective investigations have highlighted serious concerns about a possible worse outcome after endoscopic colorectal stenting as a bridge to surgery, particularly in cases of perforation. This review analyzes the most recent evidence in order to highlight pros and cons of SEMS placement in malignant large bowel obstruction.

Key Words: Colorectal neoplasm; Intestinal obstruction; Endoscopy; Self expandable metallic stents; Colorectal surgery; Chemotherapy

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Core Tip: Self-expandable metal stents (SEMS) should be considered as a primary option in palliative treatment of malignant left-sided colonic obstruction. In patients with conceivably curable left-sided colon cancer, SEMS placement as a bridge to surgery should be carefully discussed, specifically focusing on lower risk and lower permanent stoma rates, but potentially higher recurrence rates when compared to surgery. In this scenario the endoscopic expertise has a significant impact on the complication rate.

INTRODUCTION

Colorectal cancer (CRC) is the third most frequently diagnosed malignancy in the world and the second cause of cancer-related mortality[1]. About 20% of patients with CRC are admitted with this surgical emergency, which continues to be one of the most frequent causes of large bowel obstruction in adults[2-4]. Obstructive CRC most frequently develops in the sigmoid colon, with 75% of tumors located distal to the splenic flexure[5]. Emergency surgery (ES) is the typical approach for obstructive right-sided colon cancer, along with primary resection and ileocolic anastomosis[6]. However, it is debatable whether emergency or radical surgery following stenting as a bridge to surgery (BTS) should be considered for obstructive left-sided colorectal cancer[7]. Self-expandable metal stents (SEMS) for BTS have shown outstanding short-term results, but related complications such as perforations can be devastating and long-term outcomes are still a matter of debate[8-11].

STENT AS A BRIDGE-TO-SURGERY

Clinical aspects

Over the last decades, many papers have been published on colonic stenting for neoplastic obstruction, including randomized controlled trials (RCT), post-hoc analysis and systematic reviews. Moreover, in 2020 the European Society of Gastrointestinal Endoscopy (ESGE) provided updated guidelines on this topic[7]. Even though the role of SEMSs in the management of malignant colonic obstruction has been well characterized, several issues remain. Although screening programs are widespread in the developed countries, large bowel obstruction is one of the most common causes of ES in patients with CRC[7,12]. For example, in the United Kingdom, the rate of colorectal cancer presenting as an emergency remains at 20%[13]. Colonic SEMS placement is mainly suggested for patients who have obstructive symptoms and CT-results compatible with obstructing CRC. Acute colorectal obstruction (ACRO) is a medical emergency related to CRC that occurs more frequently in patients with advanced disease, in whom ES is responsible of significant morbidity and mortality than elective surgery, particularly in aged patients[14,15]. These patients usually present to the emergency department with nausea, vomiting, constipation and/or abdominal distention, often combined with poor intake of food from the previous days[16].

In ACRO, the main therapeutic aim is to decrease colon distension and prevent its complications (i.e. necrosis, perforation) that are generally associated with pneumoperitoneum and systemic inflammatory response syndrome. Therefore, colonic stenting is an interesting option to obtain this goal in ACRO, as a BTS regardless of etiology and for palliative purposes in patients with advanced and/or unfit for surgery CRC[7,15].

Effective stent deployment allows for non-surgical bowel decompression and makes it possible to prepare the colon for an upcoming elective oncologic resection. Furthermore, in CRC obstruction, the proximal colon is usually dilated and ischemic, which may increase the risk of colostomy/ileostomy if ES is performed. Many studies have shown that in this situation SEMSs may decompress the dilated proximal colon, thus obviating the requirement of ES with colostomy/ileostomy[17].

To evaluate the severity of obstruction, in Japan a modified point score system called ColoRectal Obstruction Scoring System (CROSS) (table 1) is widely used. CROSS 0 patients need ES or SEMS placement. CROSS 1 or 2 patients are candidates for elective surgery. CROSS 3 and 4 patients can receive food, therefore, SEMS placement is not necessary. A post hoc analysis of two prospective, observational, single-arm multicenter clinical trials demonstrated the short-term high efficacy and safety of SEMS placement as a BTS for patients with obstructive CRC classified as CROSS 0, 1, and 2[18].

Clinical success and adverse events

In a large cohort prospective study, the clinical success rate of SEMS placement was 95.5% and the technical success rate 97.9%. Major adverse events included perforation (2.1%), stent migration (1.0%), and stent occlusion (0.8%)[19]. The most important causes of perforation were the procedure itself (0.8%) and comorbidities (impending perforation, obstructive colitis) not manifest prior to SEMS insertion (0.6%). In a retrospective study, the technical success rate for stents placing for left-sided malignant colonic obstruction (LS-MCO) and rectal obstruction did not differ, but the clinical success rate was lower in patients with rectal obstruction (85.4% *vs* 92.1%; $P = 0.02$). In addition, the latter group of patients had a higher complication rate (37.4% *vs* 25.1%; $P = 0.01$), due to an increased risk of extra-intestinal cancer[20]. Moreover, from the literature it is well known that the technical and clinical failure rates for colonic stenting are strongly influenced by expertise, technique, lesion characteristics, and location of obstruction or anatomy of the colon, such as tortuosity[7,21]. Since there have been growing concerns about protracted and technically challenging stent placement in complex patients, the Colonic Stent Safe Procedure Research Group, in collaboration with the Japan Gastroenterological Endoscopy Society, has developed mini-guidelines to ensure the procedural safety and efficacy for colonic stent placement. A post-hoc analysis[22] of a large multicenter clinical trial identified the risk factors for difficult colonic stenting cases such as a CROSS score of 0 before SEMS placement, evidence of peritoneal carcinomatosis, tumor site in the right colon, stricture length ≥5 cm and

placement of multiple SEMSs[22]. In light of this evidence, Kuwai *et al* concluded that before attempting SEMS placement for obstructive CRC clinicians must anticipate technical challenges.

The choice of the stent

Various SEMS have been developed, but they can be generically classified as covered and uncovered. A recent meta-analysis examined the effectiveness of uncovered vs covered stents in treating colonic obstruction either as a curative BTS or palliative option. Uncovered SEMSs presented less complications (e.g. tumor overgrowth and displacement), longer SEMS patency (mean duration 18 mo), while the risk of tumor ingrowth was higher, as expected. Rates of technical success, clinical success, perforation, stool impaction and stent obstruction were similar in both groups[21].

It is difficult to make recommendations regarding the SEMS length or diameter, as few studies have shown conflicting results. When selecting a stent after fluoroscopic measurement of colonic stricture length, it is widely accepted in the clinical practice to follow a simple rule: to prepare for stent foreshortening, the distal edge of the SEMS should be placed proximal to the obstruction. Furthermore, the SEMS length should include 1-2 cm on each side beyond the stricture, considering the extent of shortening once deployed[7,17,21,23].

Is bridge-to-surgery stenting a safe alternative to emergency surgery?

Emergency surgery is burdened by high anastomotic leakage rates, estimated at 18% to 33%[12]. Furthermore a recent study suggests that emergency presentation remains an independent poor prognostic indicator after curative colorectal resection[24]. The optimal management of left-sided malignant large bowel obstruction is less clear than the right-sided cancer where the surgical approach is mostly recommended[25].

Several surgical options exist for left-sided bowel obstruction including primary resection (with or without anastomosis), subtotal colectomy (with or without anastomosis) or unfunctioning ileostomy/colostomy with interval resection[24,25].

For the first time in 1994 Tejero *et al*[26] described the technique of SEMS placement in 2 patients with ACRO as a BTS. Nearly twenty years after this initial description, the debate is still open regarding the role of SEMSs as a BTS for symptomatic LS-MCO because interpretation of the literature on this subject is still challenging.

The fundamental hypotheses driving the growing interest in SEMS placement are that it can turn ES into elective surgery, thereby reducing preoperative morbidity. Webster et al[25] analyzed 19 international guidelines for the treatment of LS-MCO from 2010 to 2018 and asked whether ES or stent placement as a bridge to surgery was the best procedure with regards to morbidity, mortality and long-term oncological outcomes. They concluded that there was a lack of high-quality evidence[25]. The more recent guidelines of the European Society of Gastrointestinal Endoscopy recommend to reserve colonic stenting in case of clinical symptoms and radiological signs of obstructing CRC, without evidence of perforation (strong recommendation, low quality evidence)[7].

In 2011, one of the first multicenter randomized trials comparing ES with colonic stenting as a BTS for left-sided CRC showed that colonic stenting had no decisive clinical advantages for global health status, mortality, morbidity and stoma rates. Moreover their results raised concerns about overt and silent perforations responsible for tumor spread[27].

A systematic review and meta-analysis of RCTs on colonic stenting as a BTS *vs* ES for acute symptomatic malignant left sided colonic obstruction[12] showed that patients treated with SEMS as a BTS had less short-term overall morbidity and reduced rates of both permanent and transient stoma. Albeit influenced by local expertise, level of obstruction and patient's clinical status, stenting as a BTS for LS-MCO showed lower risk than ES in the short-term morbidity (60 d after surgery). However, recurrence rate data between the two groups showed a clear trend in favour of ES over stenting as a BTS (26% *vs* 40%), although this was not statistically significant.

In a subsequent multicenter randomized controlled trial (ESCO trial) comparing stenting as a BTS to ES for malignant colonic obstruction, Arezzo A. *et al* reported a

similar short term complications rate between the two groups but a higher stoma rate in the ES group (P = 0.031)[28]. Looking at the long term oncologic results of the ESCO trial, no difference was observed between the two groups in terms of overall survival, time to progression and disease free survival[29]. These results have also been confirmed in a more recent meta-analysis by Cirocchi *et al*[30].

While most of the studies tried to understand if SEMS placement is more convenient than ES[12,31,32], there are few studies comparing the bridge to elective surgery approach such as decompressive stoma (DS) *vs* SEMS placement. Creation of a DS is a quite simple procedure with a near 100% success rate and can be performed in almost all patients while, as mentioned above, colonic stenting is an intervention requiring specific technical skills and expertise, including the ability to select correctly the patient basing on stricture features (length and location), and carries risks of adverse events. A population-based cohort study[33] comparing the two bridge to elective surgery approaches showed that SEMS appears to be the safest procedure, with a shorter hospital admission, as well as in palliative care. In a recent meta-analysis of seven studies (1 prospective, 6 retrospective), involving 646 and 712 patients who underwent SEMS and DS approaches respectively, Zhang *et al* found a significantly lower complication rate in the SEMS group than in the DS group (8.68 vs. 16.85%; P = 0.004), without differences in short-term mortality and permanent stoma rates. In line with the previously cited study[33], the authors concluded that SEMSs may be a better alternative to DS for obstructive CRC, but highlighted the lack of high-quality RCTs[34].

Finally, a newly published randomized trial with a longer follow-up (3 y) and larger population compared to prior studies, randomized patients with left-sided obstructive colon cancer to colonic stenting or surgical decompression. The authors showed that among patients undergoing potentially curative treatment, there were no significant differences in 30-d postoperative mortality or duration of hospital stay between stenting followed by delayed elective surgery and emergency surgery group. Moreover the use of a stoma resulted more frequent in patients treated with immediate surgery than in patients treated with SEMS (67.9% *vs* 47.5%; P = 0.003), without substantial differences

in peri-operative morbidity, intensive care use, quality of life and 3-y recurrence or mortality[35].

Timing of surgery

The proper timing of surgery subsequent to SEMS placement as a BTS is not yet clear. Adequate radial stent expansion, ischemia reversibility of the colon proximal to the stricture and colon cleansing require sufficient time after SEMS deployment. In theory, surgery can be postponed for at least 1 wk after SEMS placement to reduce the risk of stoma and postoperative complications, such as anastomotic leaks, abscesses, and wound problems. However, long delays in surgery can lead to a high rates of complications related to SEMS. Therefore, surgery is generally suggested 5-10 d after SEMS insertion[7,17].

STENT AS PALLIATIVE TREATMENT

SEMS and decompressive stoma were compared in three randomized controlled trials as palliative procedures for malignant bowel obstructions[36–38]. Palliative situations included patients unfit for surgery, as well as patients with inoperable primary lesions or metastatic disease. Given its effectiveness and the enhanced quality of life (QoL) that comes from avoiding a stoma, colonic stenting was judged to be preferable in both investigations. In a randomized prospective trial, Fiori *et al* found that the mortality and morbidity rates following palliative stenting and colostomies were comparable. However in the stenting group a shorter hospital stay, a faster return to oral intake, and a shorter operating time were recorded[37,38]. On the other hand, a Dutch trial with a similar study design was prematurely stopped because of the unacceptable high mortality rate due to perforations in the stenting group. The authors hypothesized that the unpredictable high frequency of perforation in the nonsurgical arm could be associated with the type of stent used at that time[39].

Stent and chemotherapy

Data about the effects and safety of systemic chemotherapy alone or in association with biological agents (anti-VEGF or anti-EGFR) combined with palliative stenting in metastatic colorectal cancer (mCRC) patients are lacking.

In a metanalysis including 837 mCRC patients, patients treated with SEMS had similar overall survival (OS) compared to surgery-treated patients (OS = 7.64 mo *vs* 7.88 mo respectively) and noted a shorter time before starting chemotherapy (33.36 d *vs* 15.53 d, P < 0.00001) and lower 30-d mortality (4.2% *vs* 10.5%, *P* = 0.01)[40]. Tumor response to chemotherapy can increase the rate of complications related to stent placement, such as stent migration or late perforation, but, on the other hand, can reduce the risk of obstruction by maintaining its luminal patency, especially in a palliative setting. A multicenter retrospective study included 38 mCRC patients treated with only chemotherapy; major complications related to stenting were: perforation (8%), stent migration (5%), and re-obstruction secondary to tumor ingrowths (13%)[41]. A retrospective trial including 72 mCRC patients compared long-term outcomes of palliative SEMS in patients treated with chemotherapy or with best supportive care. In the chemotherapy group, there was a higher rate of late migration (20% *vs* 2.4%, *P* = 0.018, for chemotherapy and best supportive care group respectively); patients refractory to chemotherapy reported a higher rate of late obstruction in comparison to patients who reached disease control during treatment (35.7% in disease progression, 0% in disease control, *P* = 0.014)[42]. A recent metanalysis studied the impact of systemic treatment (chemotherapy alone or in association with targeted therapy) on the risk of the complications after SEMS deployment and on outcome in terms of survival rates. Authors showed that chemotherapy was not related to a higher risk of SEMS-related complications nor a reduction in the survival rates[43].

The introduction of bevacizumab improved outcome of mCRC patients[44], although data about its effect on stent placement are still controversial. Moreover, some authors raised the hypothesis of an increased risk to develop SEMS-related complications (such as perforation) in patients on bevacizumab[45,46]. Conversely, other authors demonstrated that the addition of bevacizumab to chemotherapy did not cause a higher

perforation rate in comparison to the chemotherapy alone[47,48]. In an Italian retrospective, multicenter study including 91 mCRC patients treated with chemotherapy plus anti-VEGF or anti-EGFR agents, no correlation between chemotherapy with or without biological therapy, K-RAS status or risk of SEMS-related complications was shown[46].

These studies had several limitations: their retrospective nature, different outcomes and small sample size, patients with heterogeneous characteristics and different settings. At the state of the art more prospective and randomized trials to define the outcome and safety of the association of SEMS placement and systemic treatment are warranted.

CONCLUSION

Colonic stenting is a well-recognized palliative approach for treating malignant left-sided colonic obstruction, with high rates of technical and clinical success. Especially in patients with poor general condition and limited life expectancy, it may allow for an early hospital discharge, an improved QoL and prolonged survival in comparison to surgery.

SEMS placement as a BTS has the advantage to convert an ES into an elective one, reducing preoperative morbidity, allowing for adequate oncological staging, good colonic preparation and faster initiation of chemotherapy. Although numerous prospective and retrospective investigations have highlighted serious concerns about tumor seeding after endoscopic colorectal stent placement, particularly in cases of perforation, recent high quality studies displayed encouraging results. Operator expertise remains a key element to ensure accurate stent placement and restoration of bowel function with a low rate of complications. For this reason, this approach should be considered a standard practice only in experienced high-volume referral centers and clinicians should carefully select the patients fit for an endoscopic decompressing approach before starting the procedure.

In conclusion, to demonstrate the long-term safety of stenting as a BTS, more proof from prospective, preferably randomized trials on the risk of tumor recurrence following

stenting is necessary. Until then, the obvious short-term benefits, combined with the high mortality rate in frail and elderly patients, should be weighed against the potential long-term threats of tumor recurrence.

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