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Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Ladan Teimoori-Toolabi, MD, PhD, Associate Professor, Department of Molecular Medicine, Pasteur Institute of Iran, Tehran 1316943551, Iran.
iteimoori@pasteur.ac.ir

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Management of obstructive colon cancer: Current status, obstacles, and future directions

Ri-Na Yoo, Hyeon-Min Cho, Bong-Hyeon Kye

ORCID number: Ri-Na Yoo 0000-0002-7597-5182; Hyeon-Min Cho 0000-0002-7183-2838; Bong-Hyeon Kye 0000-0002-5251-990X.

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Ri-Na Yoo, Hyeon-Min Cho, Bong-Hyeon Kye, Division of Colorectal Surgery, Department of Surgery, St. Vincent's Hospital, The Catholic University of Korea, Suwon 442-723, South Korea

Corresponding author: Bong-Hyeon Kye, MD, PhD, Associate Professor, Surgeon, Surgical Oncologist, Division of Colorectal Surgery, Department of Surgery, St. Vincent's Hospital, The Catholic University of Korea, 222 Banpo-daero, Suwon 442-723, South Korea.
ggbong@catholic.ac.kr

Abstract

Approximately 10%–18% of patients with colon cancer present with obstruction at the initial diagnosis. Despite active screening efforts, the incidence of obstructive colon cancer remains stable. Traditionally, emergency surgery has been indicated to treat patients with obstructive colon cancer. However, compared to patients undergoing elective surgery, the morbidity and mortality rates of patients requiring emergency surgery for obstructive colon cancer are high. With the advancement of colonoscopic techniques and equipment, a self-expandable metal stent (SEMS) was introduced to relieve obstructive symptoms, allowing the patient's general condition to be restored and for them undergo elective surgery. As the use of SEMS placement is growing, controversies about its application in potentially curable diseases have been raised. In this review, the short- and long-term outcomes of different treatment strategies, particularly emergency surgery *vs* SEMS placement followed by elective surgery in resectable, locally advanced obstructive colon cancer, are described based on the location of the obstructive cancer lesion. Controversies regarding each treatment strategy are discussed. To overcome current obstacles, a potential diagnostic method using circulating tumor DNA and further research directions incorporating neoadjuvant chemotherapy are introduced.

Key Words: Colonic neoplasms; Self-expandable metallic stents; Intestinal obstruction; Survival rate; Morbidity; Mortality

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Core Tip: The optimal management of obstructive colon cancer remains intricate and

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controversial, particularly now that the use of colonoscopic stents is expanding. Several studies have demonstrated the better short-term outcome achieved by delayed surgery after self-expandable metal stent (SEMS) placement than emergency surgery. However, concerns that SEMS placement diminishes oncologic outcomes have been increasing. This article summarizes the impact of SEMS placement in managing obstructive colon cancer and suggests future research to resolve current problems.

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INTRODUCTION

Obstructive colon cancer requiring emergency surgical or procedural intervention accounts for 10%-18% of patients initially diagnosed with colon cancer[1-3]. With obstructive symptoms of nausea, vomiting, abdominal pain, and severe distension, patients often present with physical deterioration resulting from the catabolic state of muscle wasting and poor oral intake. Occasionally, patients with obstructive colon cancer have concomitant spontaneous colon perforation, a frightening complication associated with high postoperative morbidity and mortality, at either the cancer site or proximal colonic segment[4]. Moreover, the obstructive feature of colon cancer itself is an independent high-risk feature of recurrence, and patients with obstructive colon cancer tend to have an advanced cancer stage with poor prognostic factors[5]. Compared to patients undergoing elective surgery, patients requiring emergency surgery for obstructive colon cancer have worse short-term and long-term oncologic outcomes[1,2,5].

Unfortunately, despite active screening efforts, the incidence of obstructive colon cancer remains stable[3,6]. The management of obstructive colon cancer is complex and challenging due to multiple factors, including the patient's index presentation of a poor general condition, limited information regarding the cancer stage, and the need for immediate intervention in an emergency setting. This article addresses the current treatment options, difficulties, and future directions for managing obstructive colon cancer to achieve an optimal outcome.

LOCATION OF OBSTRUCTIVE CANCER LESION

It is well known that the most common cause of colonic obstruction in adults is colorectal cancer[7]. Abdominopelvic computerized tomography scans are an excellent diagnostic modality that is readily available and accurately localizes obstructive cancer lesions with high sensitivity and specificity[8]. Obstructive colon cancer is usually classified as right-sided or left-sided according to proximal or distal to the splenic flexure. Previous studies indicate that more than half of acute obstructive colon cancer occurs on the left side, most commonly in the sigmoid colon[1,6,8]. The anatomic characteristic of a narrow luminal diameter in the left-sided colon explains the higher incidence of obstructive colon cancer compared to the right-sided colon. On the other hand, a large diameter of the cecum and ascending colon allows a bulky characteristic of the tumor. Indeed, right-sided obstructive colon cancer seems more locally advanced than left-sided[3]. An obstructive cancer lesion in the rectum is the least frequent due to the sizeable luminal diameter of the rectum and the symptoms of bleeding and defecation difficulty caused by rectal cancer itself[3].

The anatomic characteristics of the colon and rectum have led to different treatment approaches depending on the obstructive lesion location. Primary tumor resection with ileocolic anastomosis has been preferred to treat right-sided cancer obstruction [9]. Generally, oncologic resection of the right-sided colon is considered less arduous. Additionally, the relatively low anastomotic complication rate, from 2.8% to 4.6%, supports primary resection and anastomosis[10]. Double-barrel entero-colostomy after primary tumor resection is an alternative for patients with a high risk of anastomotic leakage. Compared to right-sided obstructive colon cancer, left-sided colon cancer has

variable treatment options, primarily comprised of emergency primary tumor resection with or without stoma formation or decompression followed by delayed tumor resection. The choice is usually made based on the patient's general condition, availability of resources, and complete oncologic resection feasibility. In obstructive rectal cancer, optimal oncologic resection with total mesorectal excision is unobtainable. Rectal cancer that causes acute obstruction is usually locally far advanced and highly likely to invade adjacent urogenital organs, large neurovascular structures, and even bony structures. Therefore, for obstructive rectal cancer, decompression to relieve acute symptoms is more desirable than primary tumor resection to avoid serious intraoperative morbidity and suboptimal surgical outcomes. This article discusses the details regarding treatment options and the outcomes of obstructive colon cancer.

TREATMENTS AND THEIR OUTCOMES

Right-sided cancer obstruction

Traditionally, primary oncologic resection *via* right hemicolectomy or extended right hemicolectomy with ileocolic anastomosis has been advocated for right-sided obstructive colon cancer[11]. A systematic review of studies related to treating right-sided obstructive colon cancer demonstrated that 86% of patients underwent emergency resection[12]. Less strenuous surgical techniques for mobilization and resection of the right-sided colon lead many surgeons to prefer primary tumor resection in an emergency setting. Compared to colocolic or colorectal anastomosis, many surgeons pursue primary ileocolic anastomosis, even in frail patients, due to the abundant blood supply and relatively simple manipulation of the dilated proximal bowel with enough length. A recently published multicentered retrospective study on the outcomes of elderly patients treated for obstructive colon cancer revealed that 97% of patients received upfront surgery for proximal colon cancer obstruction[13]. In the study, 54% of patients were over 75 years of age. The rate of resection with primary anastomosis among the elderly patients was not different from that of the younger patients.

Not surprisingly, the short-term outcome after emergency right hemicolectomy with ileocolic anastomosis for obstructive right-sided cancer is worse than that after elective surgery for right-sided colon cancer. Postoperative morbidity after emergency surgery is reported to range from 46% to 54%[13,14]. Compared to the morbidity rate of 30% after elective right hemicolectomy for colon cancer[15], the postoperative morbidity rate after emergency surgery is much higher. The rate of anastomotic leakage after emergency surgery is reported to range from 12% to 16.4%[13,14], which is also higher than the leakage rate of 4.1% after elective surgery[16]. As expected, the postoperative mortality rate after emergency surgery is 14.5%, higher than the rate of 2.6% after elective surgery. Risk factor analysis for anastomotic leakage supports the notion that emergency surgery imposes a greater risk of anastomotic leakage and leakage-related mortality[17]. Such short-term outcomes indicate that oncologic resection with primary anastomosis for right-sided obstructive colon cancer in an emergency setting may not be as uncomplicated as anticipated.

Other surgical treatment options in an emergency setting may include the creation of loop ileostomy after resection and anastomosis, the creation of end ileostomy after resection only, the creation of loop ileostomy without resection, or enterocolic bypass surgery. For resectable right-sided obstructive colon cancer, primary tumor resection may be an optimal treatment option. In cases of unstable hemodynamics or severe intraperitoneal contamination by bowel perforation, loop ileostomy or end ileostomy is unavoidable. However, high output from ileostomy and related morbidities, such as dehydration, electrolyte imbalance, and acute renal failure, frequently occurs. Distressingly, surgeons encounter the dilemma of risking anastomotic leakage or stoma-related morbidity. For unresectable right-sided obstructive colon cancer, the creation of loop ileostomy or enterocolic bypass surgery is recommended to decompress proximal bowel dilatation, alleviating bowel obstruction symptoms[11]. Relevant studies on the treatment options for unresectable right-sided obstructive colon cancer are scarce and limited to the formation of percutaneous cecostomy, which is currently not performed due to malfunctions and complications or is reserved only for a small number of patients with very high morbidity[11,18].

Staged operation after endoscopic placement of the SEMS may offer a possible treatment option for both resectable and unresectable right-sided obstructive colon cancer. However, the technical difficulty seems to hamper the wide application of

colonoscopic stenting for right-sided colonic obstruction. Additionally, due to a lack of evidence, the use of the SEMS as a bridge to elective surgery is currently not recommended, except for patients with high morbidity[11]. Nevertheless, a newly updated systematic review comparing the treatment outcomes of staged operations after SEMS placement in curable right-sided obstructive colon cancer demonstrated that the technical success rate reached 96%, disputing the previous belief of technical difficulty[12]. Furthermore, the postoperative complication rate is approximately 30%, ranging from 7% to 44%[12,14], similar to the morbidity rate after elective surgery. After the staged operation, the rate of anastomotic leakage is estimated to be approximately 5.5%[12], comparable with the rate observed after elective surgery. The mortality rate of 1.2% after the staged operation is comparable to elective surgery[12]. The long-term oncologic outcome of right-sided obstructive colon cancer appears to be equivalent or better in patients who underwent the staged operation after SEMS insertion than in patients who received emergency surgery[19].

Current evidence provides safety and feasibility of the staged operation after SEMS insertion to treat right-sided obstructive colon cancer. However, the studies were mostly designed retrospectively with small sample sizes. Patients with unstable hemodynamics would have been excluded from the staged operation, leading to selection bias. The short-term outcome might have been related to the staged operation. On the other hand, such evidence indicates that the staged operation after SEMS placement can achieve a better short-term outcome in a certain group of patients. The selection criteria of an appropriate patient for the staged operation after SEMS placement can be suggested. Because SEMS insertion is impossible if an obstructing cancer is located in the cecum or ileocolic valve, SEMS insertion could be considered when the obstructive cancer is located beyond the cecum in the abdominopelvic computed tomography (CT) scan. Additionally, experts in colonoscopy seem to handle a long colonic length of the distal segment. Therefore, if an expert in colonoscopy is available and there is no sign of perforation on CT imaging, colonoscopic SEMS insertion may be an option before undergoing emergency surgery. After all, optimal treatment for right-sided obstructive colon cancer should be determined based on the resectability of the tumor, presence of perforation and peritonitis, and hemodynamic stability of the patient. Large-sized prospective comparative studies are necessary to obtain concrete evidence.

Left-sided cancer obstruction

Compared to those for right-sided obstructive colon cancer, treatment options for left-sided obstructive colon cancer are diverse and controversial. Conventionally, primary tumor resection with end stoma formation has been highly preferred to treat obstructive left-sided colon cancer in an emergency setting[20,21]. However, emergency surgery itself has been identified as an independent risk factor for mortality[22]. The postoperative complication rate is higher than the rate after elective surgery[8,23]. A significant number of patients end up with temporary or permanent stoma after emergency surgery. Furthermore, subsequent surgery for stoma reversal is associated with a high morbidity rate of 21% to 36%[24,25]. Up to 71% of patients never undergo surgery for stoma reversal, significantly affecting the quality of life[25, 26]. The risk factors related to nonreversal of the stoma include advanced age, a postoperative complication that occurred after emergency surgery, comorbidity, and advanced cancer stage[24,26]. Although the operative approach with primary tumor resection with end stoma is considered the safest option due to the absence of anastomotic complications[20], the two-stage operation is complex and may significantly reduce patient quality of life.

Diverting stoma is another operative procedure for damage control in acute left-sided colonic obstruction. The formation of a diverting stoma is followed by the second-stage operation of primary tumor resection with or without colostomy closure. Stoma closure can take place at a third stage. A diverting stoma may stabilize the patient's general condition and allow bowel preparation and proper staging before oncologic resection. However, patients for whom a three-stage procedure is planned may not undergo subsequent operations, even if they are considered fit. When the morbidity and mortality associated with each surgical stage are considered cumulatively, the staged operation does not provide any advantage. Furthermore, a randomized controlled trial comparing emergency colostomy followed by a staged operation to emergency Hartmann's procedure showed similar morbidity and mortality rates between two procedures; thus, the authors did not support the use of colostomy in frail patients[27]. One advantage of the staged operation is a lower rate of permanent stoma. However, patients who undergo staged operations require a more extended hospital stay for additional surgical procedures following initial colostomy

formation. Nevertheless, due to a lack of evidence, a Cochrane systematic review in 2004 could not conclude which of the two alternative approaches was the most beneficial in acute left-sided obstructive colon cancer[28].

In an emergency setting, the reconstruction of bowel continuity has been avoided in the management of acute left-sided colonic obstruction due to the risk of anastomotic leakage. However, a two-stage operation followed by Hartmann's operation has the significant disadvantage of cumulative morbidity and mortality associated with a second operation and reduced quality of life when the stoma is kept. Nonetheless, some colorectal surgeons attempted to create a primary anastomosis after emergent primary resection and demonstrated its feasibility and safety in selected patients[29, 30]. In a systematic review, Breitenstein *et al*[31] evaluated the superiority of the one-stage procedure compared to multistage procedures for left-sided obstructive colon cancer. The authors demonstrated that primary resection and anastomosis were superior to two- or three-stage operations in terms of mortality, with a relative risk difference from -2% to -27% [31]. It appeared that selection bias strongly affected the study result, in which patients with better prognoses were more likely to have a one-stage operation. Previous studies extensively investigated risk factors related to mortality and anastomotic leakage and identified high-risk conditions, such as advanced age, presence of comorbidity, advanced tumor stage, malnutrition, and presence of peritoneal contamination[22,32]. Currently, primary resection and anastomosis are the preferred options for uncomplicated left-sided obstructive colon cancer without risk factors for anastomotic leakage[11].

There are two main methods of resection, and the optimal procedure type is still debated. Segmental colonic resection with intraoperative colonic irrigation is one option, and the other is subtotal or total colectomy. Segmental resection can preserve the proximal colonic segment, but on-table lavage is time-consuming and may result in fecal spillage[33]. Subtotal or total colectomy is advocated for low risk of anastomotic leakage in ileocolic or ileorectal anastomosis[34,35]. It can eliminate the distended proximal colon with ischemic lesions and serosal tears on the cecum, reducing the risk of fecal spillage and contamination. Subtotal or total colectomy can also effectively manage synchronous tumors in the proximal colon[36]. Negative aspects of subtotal or total colectomy include the need for an experienced surgeon or subspecialist, a prolonged operation time, and a decreased bowel function[37]. In terms of morbidity and mortality, a multicenter randomized controlled trial demonstrated no differences when two different surgical procedures – total/subtotal colectomy *vs* segmental colectomy with on-table lavage – were compared[37]. Therefore, the current 2017 WSES guideline states that total colectomy is not preferred to segmental colectomy in the absence of impending perforation in the cecum, evidence of bowel ischemia, or synchronous right colonic cancers[11].

As in right-sided obstructive colon cancer, endoscopic stent placement followed by the staged operation is an alternative option frequently applied in left-sided obstructive colon cancer. Although SEMS was first introduced for palliative treatment in unresectable colorectal cancer[38], its use has been expanded to relieve colonic obstruction to avoid emergency surgery in resectable disease[39]. Its role as a “bridge to surgery” for patients with curable disease has been widely accepted because it allows planned curative resection after the adequate restoration of the patient's general condition and bowel preparation[40]. The use of SEMS appeared to decrease morbidity and mortality and the rate of stoma formation compared to emergency surgery[41]. Ultimately, its efficacy and effectiveness in reducing medical costs and improving quality of life were shown to be associated with shorter hospital stays, fewer stays in the intensive care unit, and fewer surgical procedures[41-43].

However, other studies comparing the SEMS decompression outcome to emergency surgery demonstrated controversial results in terms of morbidity, mortality, and the stoma rate. An observational study by Kavanagh *et al*[44] comparing emergency surgery to SEMS placement reported no difference in postoperative morbidity and mortality and the stoma formation rate, although technical and clinical success with SEMS placement was achieved in 91% and 83% of patients. A systematic review and meta-analysis including a total of 197 patients, 97 with SEMS placement *vs* 100 with emergency surgery, reported a clinical success rate of only 52.5% in the SEMS group in contrast to a rate of 99% in the emergency surgery group[45]. The overall complication rate and 30-d postoperative mortality rates of both groups were similar. The two groups also showed no significant difference in the permanent stoma rate or anastomotic leakage rate. In a systematic review and meta-analysis based on seven different randomized controlled trials, Huang *et al*[43] reported that the mean technical success rate was 77%. In contrast, the permanent stoma rate, primary anastomosis rate, and overall mortality rate were 9%, 67%, and 11%, respectively[43].

It appears that the location and length of an obstructing cancer lesion influence technical and clinical success[46]. The European Society of Gastrointestinal Endoscopy (ESGE) guidelines, updated in 2020, suggests that by an experienced endoscopist or under the supervision of an expert, colonic stenting should be attempted with an individually tailored method to the length of the stenosis and location of the tumor [47].

Despite the controversy, the use of SEMS is endorsed by surgeons pursuing minimally invasive elective surgery with laparoscopy[48,49]. The multimodal approach using endoscopic and laparoscopic procedures demonstrated favorable short-term outcomes in SEMS placement as a bridge to surgery, offering less invasive treatment than multistage open surgery. In a meta-analysis including eight different randomized controlled trials comparing SEMS decompression as a bridge to surgery to emergency surgery from 2009 to 2016, Arezzo *et al*[50] confirmed similar rates of morbidity and mortality in both treatment approaches. Nonetheless, SEMS decompression showed a significantly lower rate of temporary and permanent stoma and a higher success rate of primary anastomosis than emergency surgery[50]. Based on many clinical studies and other randomized controlled trials, the 2017 WSES and ESGE guidelines concluded that SEMS decompression as a bridge to elective surgery offers a better short-term outcome than immediate emergency surgery[11,47].

The long-term oncological outcome remains uncertain and rather suboptimal when SEMS decompression was compared to emergency surgery, as shown in Table 1. Several meta-analyses evaluating the oncologic outcome of patients who underwent SEMS decompression followed by elective surgery demonstrated that disease-free survival and overall survival were not significantly different from those who received emergency surgery[51]. Additionally, in the recent update of the randomized controlled trial by Arezzo *et al*[52], the 3-year overall survival, time to progression, and disease-free survival of the patients with SEMS decompression as a bridge to surgery were not significantly different from those of the patients with emergency surgery. However, the meta-analysis of eight different randomized controlled trials by Yang *et al*[53] showed that patients with SEMS decompression presented a higher tumor recurrence rate than patients with emergency surgery, with an odds ratio of 1.79 (95% confidence interval 1.09–2.93). Another meta-analysis of seven randomized controlled trials by Foo *et al*[54] demonstrated that the overall recurrence rate in the SEMS decompression group was higher than that in the emergency surgery group, at 37.0% and 25.9%, respectively. Although the 3-year overall survival and disease-free survival were not different between the two groups, the risk ratio of systemic recurrence was 1.627 for the SEMS decompression group[54]. Nevertheless, available data are limited, and the sample size is inadequate to draw a firm conclusion on the long-term oncological outcome of SEMS decompression as a bridge to surgery. The ESGE guidelines currently recommend that decision-making for individual patients be influenced by the relative importance of particular endpoints, either short-term outcomes or long-term outcomes[47]. Patients should be informed within a shared decision-making process to use SEMS decompression as a bridge to surgery in potentially curable left-sided obstructive colon cancer regarding a potentially higher risk of recurrence[47].

PITFALLS OF THE SEMS DECOMPRESSION FOLLOWED BY DELAYED OPERATION

Stent-related complications are a vital issue to address. A previous randomized controlled trial comparing SEMS placement to emergency surgery in left-sided obstructive colon cancer was terminated prematurely due to a high technical failure rate of 53.3%[49]. As the most lethal complication, colonic perforation during the procedure was the main reason for the premature closure of the trial. Other complications include stent migration, failure to expand within the colonic lumen, bleeding, and subsequent reobstruction[46]. The rate of colonic perforation related to stent placement was reported to be as high as 12.8%[55]. Stent migration and bleeding occur less frequently at a rate of 0% to less than 5%[55,56]. As expected, colonic perforation during the procedure, failure to self-expand, or bleeding requires emergency surgery, which may lead to mortality directly related to SEMS placement. Currently, the 30-d stent-related mortality is estimated to be 4%[46].

Stent-related perforation has not only an imminent mortality risk but also existing concerns about its implication in worsening oncological outcomes. In a recent systematic review and meta-analysis evaluating the oncological outcome of patients

Table 1 Oncological outcome after self-expandable metal stent placement as a bridge to surgery vs emergency surgery in malignant colonic obstruction

Ref.	Year	Study population	Study design	Location of obstructive cancer	Survival outcome
Matsuda <i>et al</i> [75]	2015	<i>n</i> = 1136: (1) BTS = 432; and (2) ES = 704	Meta-analysis: (1) 2 RCTs; (2) 2 prospective nonrandomized comparative studies; and (3) 7 retrospective comparative studies	Right- and left-sided	(1) No difference in disease-free survival and overall survival; and (2) No difference in recurrence
Ceresoli <i>et al</i> [76]	2017	<i>n</i> = 1333: (1) BTS = 688; (2) ES = 655	Meta-analysis: (1) 5 RCTs; (2) 3 prospective nonrandomized comparative studies; and (4) 9 retrospective comparative studies	Left-sided	(1) No difference in local recurrence and overall recurrence; (2) No difference in 3-yr and 5-yr recurrence; and (3) No difference in 3-yr and 5-yr mortality
Yang <i>et al</i> [53]	2018	<i>n</i> = 497: (1) BTS = 251; and (2) ES = 246	Meta-analysis: 8 RCTs	Left-sided	Higher tumor recurrence rate in BTS with an odds ratio of 1.79, 95%CI: 1.09–2.93
Amelung <i>et al</i> [51]	2018	<i>n</i> = 1919: (1) BTS = 938; and (2) ES = 981	Meta-analysis: (1) 5 RCTs; (2) 4 prospective nonrandomized comparative studies; and (3) 12 retrospective comparative studies	Left-sided	(1) No difference in locoregional recurrence and overall recurrence; (2) No difference in 3-yr and 5-yr disease-free survival; and (3) No difference in 3-yr and 5-yr overall survival
Foo <i>et al</i> [54]	2019	<i>n</i> = 448: (1) BTS = 222; and (2) ES = 226	Meta-analysis: 7 RCTs	Left-sided	(1) Overall recurrence rate: 37.0% in BTS vs 25.9% in ES; (2) The risk ratio of systemic recurrence 1.627 for BTS; and (3) No difference in 3-yr overall survival and disease-free survival
Arezzo <i>et al</i> [52] (ESCO trial)	2020	<i>n</i> = 115: (1) BTS = 56; and (2) ES = 59	RCT	Left-sided	No difference in 3-yr overall survival, time to progression, and disease-free survival

BTS: Bridge to surgery; ES: Emergency surgery; RCT: Randomized controlled trial; CI: Confidence interval.

who experienced stent-related perforation in an attempt at SEMS decompression, patients with stent-related perforation demonstrated significantly higher rates of global recurrence and locoregional recurrence than patients without perforation, although stent-related perforation did not influence the survival outcome [57]. A significantly increased risk of systemic and locoregional spread of the tumor was also observed in a previous meta-analysis by Foo *et al* [54,57]. Indeed, the current guidelines do not state SEMS decompression as a bridge to surgery as the treatment of choice in a potentially curable disease but consider it only as an alternative to emergency surgery in patients with an increased risk of perioperative morbidity and mortality, despite its better short-term outcome [11,47].

Several background theories explain the increased risk of tumor recurrence. First, the manipulation of a tumor during colonoscopy can cause the dissemination of cancer cells into peripheral circulation by mechanical compression of the guidewire and air insufflation, violating the principle of oncologic treatment [58]. Additionally, an increase in interstitial pressure within the tumor may cause tumor embolism in the lymphatic channels, resulting in lymphatic invasion [59]. Moreover, clinical or silent, stent-related perforation would promote cancer spread inside the peritoneal cavity, leading to locoregional and peritoneal metastasis [60]. Such arguments are supported by clinical correlations with pathologic findings, of which surgical specimens from patients with SEMS decompression presented a higher rate of perineural and lymphatic invasion [61]. In a recent systematic review and meta-analysis by Balciscueta *et al* [60], patients who underwent SEMS decompression had a significantly higher risk of perineural and lymphatic invasion, with odds ratios of 1.98 and 1.45, respectively. The authors claim that stent placement as a bridge to surgery modifies the pathologic characteristics, including perineural and lymphatic invasion, which may worsen the long-term prognosis, raising the risk of global recurrence by 1.7 times the locoregional recurrence and carcinomatosis by 2.4 times [60]. However, pathologic findings of perineural and lymphatic invasion are often observed in obstructive colon cancer. From the available data, the significant influence of pathologic changes on survival outcomes is ambiguous. However, data on survival outcomes still lack a firm conclusion. Further translational research on how disruption in the microenvironment of tumors affects locoregional and systemic metastasis may delineate SEMS decompression's effect on survival outcome.

OPTIMAL INTERVAL BETWEEN SEMS PLACEMENT AND ELECTIVE SURGERY

The time interval between SEMS placement and elective surgery remains uncertain in the current management of obstructive colon cancer. At present, prospective comparative data on how the different intervals affect the short- and long-term outcomes are not available. Two retrospective studies have reported conflicting results regarding resection timing after decompression for postoperative morbidity and oncologic outcomes[62,63]. A retrospective study using the Dutch nationwide cohort demonstrated that surgery within 5–10 d resulted in a longer hospital stay, a lower rate of laparoscopic resection, and a higher rate of stoma creation than surgery after 11 d[63]. Additionally, stent-related complications were most frequently observed in patients who underwent surgery after 17 d[63]. On the other hand, a multicenter retrospective study on the optimal timing of elective surgery after SEMS placement by Kye *et al*[62] supports the concept that early elective surgery within seven days after SEMS placement correlates with better oncological outcomes than elective surgery after seven days. Currently, the ESGE guidelines state only that the time interval for surgery after SEMS placement should balance stent-related adverse events and surgical outcomes[47]. Further investigation is necessary to determine the optimal time interval between SEMS placement and elective surgery.

ROLE OF CIRCULATING TUMOR DNA

The development of genomic sequencing technology and molecular diagnostic testing has allowed the detection of tumor-specific DNA in peripheral blood samples, suggesting the new diagnostic concept of “liquid biopsy”[64]. Circulating cell-free DNA (cfDNA) is derived and released from apoptotic or necrotic cells, and circulating tumor DNA (ctDNA) with tumor-specific DNA from tumor cells undergoing apoptosis or necrosis is released into the systemic circulation[65]. Diagnostic strategies measuring ctDNA are under active investigation for clinical application in screening, diagnosis, and predicting tumor response or resistance to treatment[65]. The concentration of ctDNA in the bloodstream represents the tumor burden in individuals; thus, its use is highly accurate and valued as a biomarker for therapeutic monitoring[65,66].

Applying the concept of therapeutic monitoring, Takahashi *et al*[67] evaluated ctDNA concentration changes after SEMS decompression to test whether SEMS placement disturbs the tumor microenvironment, causing cancer spread. In a prospective observational study, the authors observed that SEMS placement increased the ctDNA concentration in 83% of cases, indicating that SEMS placement inherently induces tumor manipulation and disruption[67]. The authors suggested that stent-induced tumor manipulation may worsen the prognosis of patients with obstructive colon cancer[67]. However, the effect of an increased ctDNA concentration on prognosis is still under investigation. A long-term follow-up study with a larger cohort is required to determine the effect of increased ctDNA on oncological outcomes.

Furthermore, the ctDNA concentration change pattern may help decide the timing and type of subsequent treatment. In the study by Takahashi *et al*[67], the ctDNA concentration changes after SEMS placement showed an increase in concentration over time. This finding implies that the longer time interval between SEMS placement and elective surgery may result in a more unsatisfactory oncological outcome. Since stent-related complications occur mostly within seven days, a short interval after SEMS placement should be considered to minimize its impact on the survival outcome[47]. On the other hand, a long interval may optimize the patient’s general condition and reduce the risk of postoperative complications[47]. Serial measurement of the ctDNA concentration may help decide the optimal timing for elective surgery for individual patients considering the long-term outcome.

APPLICATION OF NEOADJUVANT SYSTEMIC CHEMOTHERAPY IN OBSTRUCTIVE COLON CANCER

Neoadjuvant chemoradiotherapy has proven its benefit of downstaging tumors and reducing the local recurrence rate in locally advanced rectal cancer[68]. Recently, there has been a growing body of literature on the use of neoadjuvant chemotherapy before and after neoadjuvant concomitant chemoradiotherapy in locally advanced rectal

cancer for early control of micrometastasis, an increase in the complete response rate, conservative surgery with organ preservation, and an increase in adherence to chemotherapy[69]. In colon cancer, since the mainstay of treatment for the potentially curable disease is complete oncologic resection, it is rare to find studies evaluating the effect of neoadjuvant chemotherapy, and only a few studies have been conducted to evaluate its safety[70-72]. The use of neoadjuvant chemotherapy after SEMS placement in patients with potentially curable obstructive colon cancer is rare. Only one retrospective analysis with a small sample size ($n = 9$) was found[73]. In this study, the efficacy and safety of SEMS insertion followed by neoadjuvant chemotherapy and elective surgery were evaluated, and the study results revealed relatively low toxicity, high adherence to two to three cycles of neoadjuvant chemotherapy before elective surgery and no evidence of perineural invasion in resected specimens[73]. The authors suggested that neoadjuvant chemotherapy may lower the risk of perineural invasion, possibly improving survival outcomes[73]. In the FOXTROT trial, a randomized controlled trial evaluating the efficacy of neoadjuvant chemotherapy in locally advanced colon cancer, a few patients underwent SEMS placement as a bridge to surgery, and the results showed a significant decrease in the R1 resection rate and a nonsignificant trend toward better oncological outcomes at two years[70]. However, it is difficult to draw meaningful conclusions about the effect of neoadjuvant chemotherapy after SEMS placement from these studies.

In obstructive colon cancer, the ESGE guidelines updated in 2020 recommend that the treatment strategy of SEMS placement followed by neoadjuvant chemotherapy is occasionally used in patients with stage IV disease for the early and safe introduction of systemic chemotherapy[47]. In a review article, Matsuda *et al*[74] suggested that systemic chemotherapy after SEMS placement may be an optimal treatment for patients with unresectable metastatic disease who are unfit for emergency surgery. However, the authors warned of delayed stent-related complications that require strict monitoring[74]. Additionally, the use of bevacizumab should be avoided because bevacizumab is a risk factor for stent-related perforation[74]. Nevertheless, for patients with stage IV obstructive colon cancer, an optimal outcome of upfront treatment for colonic obstruction would require immediate symptomatic control and minimizing complications related to emergent treatment for subsequent treatment for systemic disease. A personalized treatment approach should be implemented to achieve the ultimate result in an individual patient.

Perhaps an observational study utilizing a serial measurement of ctDNA concentration may help determine the efficacy of this treatment approach by decreasing the ctDNA concentration following neoadjuvant chemotherapy. A well-designed, randomized controlled trial evaluating the effect of neoadjuvant chemotherapy on the short- and long-term outcomes of SEMS placement followed by neoadjuvant chemotherapy and elective surgery in potentially resectable colon cancer would provide an ample amount of information regarding the management of obstructive colon cancer.

CONCLUSION

This article summarizes the current treatment strategies for obstructive colon cancer. Clinicians and surgeons often encounter complicated decision-making processes with complex and controversial treatment strategies. Decisions should be made based on the patient's index presentation of the general condition and risk factors that affect the short-term outcome. For the long-term outcome, it would be wise to implement a treatment approach that may induce a better oncological response in individual patients. Nevertheless, a diagnostic method for monitoring treatment response is still lacking. Clinical application of ctDNA analysis may offer new insights into individualized therapeutic strategies. Although several obstacles and preconditions should be resolved, incorporating neoadjuvant chemotherapy may be a viable option for effective systemic control of micrometastasis in selected patients. After all, further investigation on the implementation of neoadjuvant chemotherapy in the treatment of obstructive colon cancer is required.

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