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Endoscopic Placement of Stents for Malignant Colorectal Obstructions: Differences in Clinical Outcomes after Elective and Emergency Procedures

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Abstract

Colorectal cancer can arise with acute obstruction that represents a potentially life-threatening condition that needs an emergency treatment for decompression. The advent of Self Expandable Metal Stents (SEMS) has changed the paradigm of treatment of this patient, limiting the appeal to emergency surgery. Nevertheless, clinical data from the most recent studies are conflicting and have generate a debate on the use of SEMS because of the uncertain effects from the oncological point-of-view. In this review we try to draw the state of art for the use of SEMS for obstruction due to colorectal cancer, both in the setting of palliation and bridge-to-surgery, focusing on data on short-term and long-term clinical outcomes.

Keywords: Colorectal Cancer; Colorectal Obstruction; Colorectal Stent; Outcomes; Self-Expandable Metal Stents

Introduction

Acute malignant large bowel obstruction represents an urgent condition characterized by pain, vomiting, hydroelectrolytic alterations and which can be complicated by ischemic and septic events that can lead to death. Poor clinical conditions in this situation may increase the risk of complications in the patient undergoing to emergency surgery. Acute occlusion is the first manifestation in 8% to 29% of cases of colorectal cancer [1]. Patients with large bowel obstruction have a worse prognosis and their management with emergency surgical decompression is associated with high morbidity and mortality rates [2]. In recent years, the use of Self-Expanding Metal Stents (SEMS) has been considered a valid alternative to emergency surgery for bowel decompression because of the high rates of success and low rates of complications [3], so that the endoscopic treatment spread out in the last decade. However, while its use is largely consolidated for palliation in patients with unresectable disease or patients unfit for surgery, its use as bridge to elective surgery in patients with potentially resectable disease has been largely downsized and is still under debate. Although less invasive than a surgical treatment, SEMS placement indeed is not free of complications, the most feared of which is perforation during and after stenting. When occurred in patients potentially resectable, perforation can determine a spreading of disease that can compromise oncological outcomes. Indeed, the most recent ESGE guidelines [4] indicate that the insertion of SEMS as a bridge to surgery is not recommended as a standard treatment for neoplastic colon obstructions, but this option should be limited to those patients with left-side colonic occlusions with an increased risk of postoperative mortality (ASA III and/or age > 70 years). The use of SEMS in proximal obstructions (proximal lesions to splenic flexure) showed conflicting results [5-7] so that guidelines [4] consider stent placement a valid alternative to surgery only for palliation. In patients with potentially curable proximal disease, indeed, surgical resection remains the gold standard [4]. The presence of perforation, peritoneal carcinosis, tight stenosis of the anal sphincter, lesions less than 5-6 cm from the anal orifice, instead, are considered contraindications to the use of SEMS [8].

Two types of SEMS are available: covered and uncovered stents. They both demonstrated to be equally effective and secure [4], although some studies showed that uncovered ones have a lower risk of migration [9,10]. On the contrary, their main limitation is the higher tumor ingrowth rate, as they are recolonized by the neoplasm with subsequent recurrence of the occlusion [11]. Moreover, the outcome of stent placement is highly influenced by the stent's diameter that should be grater that 24 mm [12]. For a correct insertion, the stent should also be positioned 2 cm upstream e downstream of the lesion [13]. Hence, the choice of the length of the stent should take into consideration both the length of the stricture and the shortening of the stent after the deployment.

Discussion

SEMS and Palliation

Palliation represents the main indication to colonic stenting for obstruction due to colorectal cancer [4]. According to data of two meta-analysis [14,15], the technical success rates ranged from 88-100%. Although the conflicting results, the use of SEMS for palliation is recommended also for proximal obstructions [4]. A recent retrospective multicenter cohort study on palliation in patients affected by obstructing proximal colon cancer [16] showed higher technical and clinical success rates for emergency surgical treatment than SEMS. However, surgery had higher hospital stays and higher rates of early Adverse Events (AEs), so that author concluded that SEMS remains the first therapeutical option in this setting and surgery should be reserved in case of failure of endoscopic treatment. Short-term outcomes. Two meta-analysis showed the advantages of SEMS compared to palliative surgery [14,15]. Stent placement, indeed, is associated to a shorter duration of hospitalization and lower rates of admission to intensive care unit (0.8% vs 18%) [14,15] when compared to surgery. However, the same studies [14,15] outlined that the patients treated surgically had a rapid regression of symptoms related to obstruction, that was significantly higher than in patients treated endoscopically (100% versus 93%). The successful deployment of the stent, indeed, it is not associated to decompression in all patients, suggesting that both technical and clinical outcome can be influenced by the length and the angulation of the stricture: shorter stricture and wider median colonic angulation distal to the stricture are positively correlated to better outcomes [17]. Nevertheless, a recent study by Nitta, et al. [18] showed that SEMS placement was associated to a rapid improvement in symptoms, with a recovery of the oral intake after a median of 2.1 days after stent placement. Moreover, the 30-days mortality rates is about for 4% in case of use of SEMS, while it rank 11% for emergency surgery [15].

Not secondarily, in case of emergency surgery the rate of stoma formation is higher than for palliative SEMS (13% vs. 54%) [15] decreasing significantly the quality of life of patients. An English observational study [19] considered 173 patients who have been subjected to emergency surgery with stoma formation and 172 treated with stent placement, demonstrating higher perioperative and postoperative complications in the stoma-group. Notably, the SEMS-group had a lower number of patients that died in hospital (6,4% vs 12,7%). Almost 13% of patients treated with SEMS placement have a complication within 30 days [19]. Early complications are mainly represented by perforation and stent migration. Perforation occur in 4-7% of cases [17,20] and seems to be related to longer strictures [17]. Migration occur in 4-10% of cases and is more frequent in the first 24 hours [15,20,21]. The risk of migration seems to be higher for fully-covered SEMS, stent with a diameter < 24 mm and previous balloon dilation [9,10,22]. Usually, most migrations are distal and can be safely managed endoscopically. Moreover, the use of SEMS for palliation allows an earlier beginning of chemotherapy, usually within 16 days, compared to 33 days in case of palliative surgery [15,21], having potential consequences on long-term oncological outcome. However, the concomitant bevacizumab-based chemotherapy is associated to an increased risk of colic perforation in patients treated endoscopically [23,24] so that the use of SEMS for palliation is not recommended in those patient that should be considered or are being treated with antiangiogenic therapy, such as bevacizumab [4].

Long-term outcomes. While short-term complications are more frequent in patients treated with palliative surgery, palliative SEMS seems to be related to higher rates of late complications [15]. The most common late complication is re-obstruction, that may occur in 18% of patients [8,19,25], usually due to tumor ingrowth, although fecal impaction and mucosal prolapse are also possible causes. The rates of re-obstruction are higher for uncovered SEMS than for fully-covered SEMS (7.8% versus 4.7%) [10,26] and this difference is probably due to the lower rate of tumor ingrowth for covered stents (0.9% versus 11.4%). The median stent patency in the setting of palliation vary widely from different studies, between 55 days and 343 days, with a median of 106 days [27-29]. In their study, Nitta, et al. [18] found out that palliative stent re-occlusion is likely to occur within one year, with 69.2% of patients that maintain stent patency until the end or follow-up or death. This data differ from previous study that reported that 80% of patients preserve stent patency till death [4]. Usually, stent re-obstruction can be safely managed endoscopically. The first choice of treatment is stent-in-stent procedure, that consists in the deployment of a second stent into the obstructed stent, obtaining a clinical success in 75-86% of patients [4,29,30]. Two other chances of treatment are balloon dilation and argon laser therapy, although less used [31]. The overall morbidity is similar between patients treated with SEMS placement and palliative surgery, that rank 34% and 38% respectively [15,21], although in case of SEMS insertion the rates of colostomy/ileostomy is lower (13% versus 54%).

SEMS as Bridge to Surgery

The use of stent as bridge to surgery has been proposed as an alternative to emergency surgery for occlusive and potentially curable colorectal cancer. Although the encouraging results from previous studies, the most recent guidelines do not recommend the use of self-expandable metallic stent as bridge to surgery as a standard treatment for colon malignant obstructions [4]. The pre-operative stent insertion in potentially curable disease is suggested as a valid alternative treatment only for those patients with symptomatic left-sided malignant colonic occlusion with high surgical risk: patients older than 70 years and/or with ASA score > III [4,32]. These patients, indeed, are often elderly and affected by several pre-existing comorbidities, so that the acute occlusion can precipitate the already precarious conditions and the emergency surgery can be burdened by severe peri- and post-operative complications and higher mortality rates. The rational of stenting as "bridge-to-surgery" is to obtain the decompression due to the acute obstruction, in order to avoid an urgent surgical intervention and allow elective surgery. The 30-day mortality, indeed, is significantly higher after emergency surgery (14,9 %) when compared to elective surgical management, respectively 14.9% and 5.8% [33]. Standing on meta-analysis [34] the mean technical success rate for SEMS as bridge-to-surgery is 76,9%, without differences in post-operative mortality comparing SEMS as bridge-to-surgery and emergency surgery. Because of the lower rates of success for SEMS placement, in those cases of right-sided occlusion in potentially curable tumors one-stage surgery with resection followed by the primary anastomosis remains the gold standard and guidelines do not recommend the use of stenting as-bridge-to-surgery [4,35]. A recent review comparing conventional emergency surgery (resection and primary anastomosis) with stent placement followed by elective resection for right-sided colonic obstructions showed a mortality rate of 10,8% in the first group and of 0% in the second [36]. However, when SEMS placement as bridge-to-surgery is indicated, guidelines weakly recommend performing elective surgery at a time interval of 5-10 days, in order reduce stent-related complications that may compromise subsequent surgery and the oncological outcome [4,37].

Short-term outcomes. Data on outcomes of SEMS as bridge-to-surgery are conflicting and vary from different meta-analysis, depending if they include only Randomized Control Trials (RCTs) or both randomized and non-randomized studies. A recent syste-matic review and meta-analysis [34], considering only RCTs, eva-luated the efficacy and safety of colonic stenting as a bridge to surgery compared with emergency surgery. SEMS placement as a bridge to surgery followed by elective surgery showed a lower overall postoperative morbidity (33.1% vs. 53.9%), higher prima-ry anastomosis rate (67.2% vs. 55.1%,) and lower stoma rate (9% vs. 27.4%,) when compared to emergency surgery in left-sided obstruction due colorectal tumors. However, the overall postoperati-ve mortality was similar after SEMS insertion as a bridge to surge-ry and emergency surgery, respectively 10.7% and 12.4%. Similar results were also found in other studies that highlighted an higher primary anastomosis rate and a lower overall stoma rate in pa-tients treated with SEMS placement as bridge-to-surgery, without increasing the risk of anastomotic leak or intra-abdominal abscess [38,39]. Kwak, et al. showed post-procedural complication were 9,5% in SEMS group and 17,7%, emergency surgery group, although no patient had permanent stoma in both groups [40]. The postoperative hospital stay was lower in the SEMS group than in the immediate surgery group (9 days in media vs 12 days, $p<0,001$), but no significant differences there were in 30-days mortality rate [41,42]. Nevertheless, patients treated with immediate surgery underwent to more stoma formation (43,1 % vs 22,9% $p<0,001$) [42].

In the setting of bridge-to-surgery the risk of perforation should be evaluate because of its important consequences on the oncological outcome. The use of SEMS and the occurrence of tumor perforation, indeed, were identified to correlate with worse overall survival [43]. The overall risk of perforation is around 5% [44] and when occurred, perforation is associated to worse long-term outcome, especially recurrence of the disease [43].

Long-term outcomes. The main controversies related to the pre-operative use of the SEMS for potentially resectable and curable disease concern long-term results. The first doubts after the initial enthusiasm were moved in some studies that showed the increased risk of neoplastic dissemination derived from the preoperative treatment of malignant occlusion with SEMS [45]. During stent placement, indeed, may occur micro-perforations and squeezing of the tumor, favoring neoplastic cells diffusion [46,47]. Maruthachalam, et al. demonstrated that patients affected by colorectal cancer and treated with stent insertion had higher levels of CEA and mRNA expression of CK20 in the blood circulation. This was probably due to manipulation of tumor during insertion of the guidewire and to tissue damage given by stent dilation [45]. A higher rate of local recurrences emerged in RCT comparing oncological medium-term outcomes in SEMS before surgery versus primary surgical resection [48]. In a retrospective study of 2013 the use of SEMS as bridge to surgery was related to a worse of overall survival [49]. However, a recent Italian meta-analysis considering 13 studies and 1089 patients showed no differences in both local and systemic recurrences between SEMS as bridge-surgery and emergency surgery. The 3-year and 5-year mortality, indeed, were similar between the two groups [50]. Several meta-analysis comparing long-term outcomes in stenting as bridge-to-surgery and emergency surgery demonstrated that the oncological outcome, determined as overall survival, disease free-survival and neoplastic recurrence, was comparable between the two groups [9,42,51,52].

Conclusions

Endoscopic placement of stents for malignant colorectal obstructions is a safe and effective procedure. However, although it is usually performed in emergency, its correct use has to consider the stage of disease, patient's comorbidities, and the potential or concomitant chemotherapy, in order to ensure the best oncological outcomes. Therefore, current indications [4] for colorectal SEMS placement include palliation for colonic obstruction by primary CRC and placement as a bridge to surgery only in those patients with high surgical risk, such as those with an ASA classification ≥III and aged over 70 years. While the use of palliative stenting is recommended both for left-sided and proximal obstructions, in case of potentially curable disease, stent placement is discouraged in right-sided neoplasia because of the lower rates of technical success and the conflicting results on clinical outcomes. Furthermore, in the setting of palliation, the use of SEMS is not recommended in those patient that should be considered or are being treated with antiangiogenic therapy, because of the higher risk of perforation. The uncertain results on long-term outcomes, limited in last years the use of SEMS as bridge-to-surgery, notwithstanding the potentially benefits on the short-term outcomes. However, evidences in the setting of SEMS as bridge-to-surgery are still lacking and further studies are needed in order to better evaluate the detainee the oncological outcome and to define the best time interval for the subsequent elective surgery.

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