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ORIGINAL ARTICLE

Delay of surgery after stent placement for resectable malignant colorectal obstruction is associated with higher risk of recurrence

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Abstract
Background Self-expanding metal stents can be used as bridge to elective surgery for acute malignant colonic obstruction. However, the impact on long-term oncological outcome and the optimal timing of surgery are still unknown.
Method This was a retrospective multicenter study performed at four colorectal centers. Patients undergoing stent placement as bridge to surgery, between January 2010 and December 2013, were included in the study. Primary outcomes were survival and recurrence rates along with location of the metastases. Additionally, we recorded time from stent placement to elective surgery. Secondary outcomes were postoperative complication rates. Complications were classified according to the Clavien-Dindo classification score. A logistic regression model was used to describe impact of delayed stent removal on risk of recurrence.
Results This study included 112 patients, with a median follow-up of 43 months. Survival rate was 70%. We found a recurrence rate of 37%, primarily local recurrences (17%). Procedure-related complications at the stent placement were seen in 18%, and complications after subsequent elective surgery were seen in 39%. A significantly higher risk of recurrence with increased time from stent placement to elective surgery (OR 5.1 [1.6–15.8], $p = 0.005$) was found.
Conclusion Delay of elective surgery after stent placement may have a negative influence on long-term oncologic outcomes.

Keywords Self-expandable metal stents · Oncological outcome · Bridge to surgery

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Introduction

Colorectal carcinoma is the third most common type of cancer. It has been reported that 8–40% of all patients with colorectal carcinoma present with acute malignant obstruction [1–3]. Self-expanding metal stent (SEMS) was introduced in the 1990s as an alternative to emergency surgery [2]. SEMS can restore luminal patency as a definitive palliative treatment or as a bridge to elective surgery. The expected benefit of SEMS as a bridge to surgery is the opportunity to optimize the patient's clinical condition before surgery, with less morbidity, mortality, and need for a stoma [2, 4].

However, a meta-analysis of randomized controlled trials failed to show beneficial effects of SEMS compared with emergency surgery, regarding morbidity and mortality [4]. Furthermore, a recent study found SEMS to be related to worse overall and disease-free survival compared with emergency surgery [5]. In addition, a higher rate of local recurrence after SEMS compared with emergency surgery has also been shown [6]. Although SEMS is frequently implemented as an alternative to emergency surgery in the management of colonic obstruction, little is known about the impact on long-term oncological outcomes and the optimal time for the elective procedure with resection of the obstructed colon. Longer duration of stent placement may result in an increased risk of microperforation or induce a local response that may result in poorer oncological outcome.

We aimed to investigate the long-term oncological outcome after stent placement as bridge to surgery. Additionally, we planned to investigate if time from stent placement until tumor resection was related to recurrence rate.

Method

A retrospective multicenter study was conducted according to the STROBE statement for observational studies [7]. This study included four Danish colorectal centers. Medical records, from January 2010 to December 2013, of patients undergoing SEMS placement for acute malignant obstruction were reviewed. Only patients with potentially curable colorectal cancer at time of stent placement were included in the analysis. Patients undergoing SEMS placement, as a palliative treatment, were excluded. Bridge to surgery was defined as scheduled elective surgery at the primary stent treatment or in the immediate period hereafter, independent of time between SEMS insertion and surgery.

Stent placement

SEMS insertions were performed by a combined endoscopic and fluoroscopic approach. All procedures were carried out under general anesthesia or conscious sedation. SEMS insertion across the obstruction was performed according to the standard technique as previously described [8–10]. A guidewire was introduced over the stenosis and beyond the obstruction, and a stent was deployed over the guidewire. Correct positioning of the stent was confirmed by fluoroscopy. Stents used were WallFlex (colonic stent; Boston Scientific), Hanarostent (M.I. Tech., Seoul, Korea), and Evolution (Cook Medical, IN, USA). After SEMS placement, patients were offered an elective resection.

Data recorded

Following demographical data were retrieved: gender, age, TNM stage, adjuvant chemotherapy, American Society of Anesthesiologist (ASA) score, tumor location, and type of stent. Furthermore, time from SEMS placement to elective surgery, 30-day survival rate, 1-year survival rate, and complications were recorded. Complications were classified according to Clavien-Dindo classification [11]. Finally, we registered recurrence rate and the location of the metastasis. Local recurrence was defined as cancer in the same place to the original cancer or very close to it. Local recurrence could be solid tumors or diffusely peritoneal. In systemic metastasis, the cancer had spread to organs or tissues far away from the original cancer. Patients were followed until death or May 2015.

Statistical analysis

Demographic data were presented as absolute numbers with percentages, unless indicated otherwise. The unadjusted relationship between outcome and delayed stent removal was assessed using an independent χ^2 test. A multiple logistic regression model was used to describe the independent effect of delayed stent removal on the risk for metastasis controlled for potential confounders (gender, age, tumor grade, and chemotherapy). Outcomes were presented as odds ratios (OR) with 95% confidence limits. Statistical significance was considered for $p \leq 0.05$.

All data analyses were performed using SPSS statistics, version 23.0 (SPSS, Inc.).

The current study was approved by the Danish Data Protection Agency (REG-74-2015).

Results

From January 2010 to December 2013, a total of 112 patients underwent stent placement as bridge to surgery at the four included colorectal centers. There were 56 (50%) females and 56 males, with a mean age of 71 years. Patients' demographical data are summarized in Table 1. Time from stent placement to tumor resection ranged from 0 to 165 days with a median of 18 days. Of the 112 patients, 20 (18%) had an emergency surgery due to a stent-related complication,

Table 1 Demographics

Characteristics	$n = 112$
Gender, female	56 (50)
Age, year, mean (SD)	71 (12)
Tumor location	
Hepatic flexure	4 (3.6)
Transverse colon	4 (3.6)
Splenic flexure	11 (9.8)
Descending colon	13 (11.6)
Sigmoid	68 (60.7)
Rectum	11 (9.8)
T stage	
1/ 2/ 3/ 4	0(0)/ 6(5)/ 71(63)/ 30(27)
Missing	5 (5)
Lymph node metastasis	58 (52)
Missing	5 (5)
Adjuvant chemotherapy	50 (45)
ASA score	
1/ 2/ 3/ 4	14(13)/ 61(55)/ 15(13)/ 2(2)
Missing	20 (18)

ASA American Society of Anesthesiologists

primarily migration and perforation (Table 2). Complications after tumor resection were seen in 44 (39%) patients. A 30-day survival rate at 106 (95%) was found, and at 1-year follow-up, the survival rate was 101 (90%). At the final follow-up (median 43 months), the survival rate was 78 (70%). Results are summarized and complications are classified according to Clavien-Dindo in Table 2.

Oncological outcomes

An overall recurrence rate of 41 (37%) was recorded. Of these, 19 patients had local recurrence of which 11 were solid tumors and eight were diffuse peritoneal metastases. Liver metastasis was found in 17 patients, and metastasis located in the lungs was found in 13 patients. In four cases, the metastasis was found in other locations. In one case, the metastasis was found in the columna, in another case in the kidney, and additionally, a case with metastasis in the esophagus. Finally, one patient had metastasis in her breast and retroperitoneum and cutaneous metastasis. Results are summarized in Table 2.

We investigated time from stent placement to elective surgery related to the risk of recurrence, controlled for gender, age, tumor grade, and postoperative chemotherapy. Median time from SEMS insertion to surgery was 18 days. We divided the patients in two groups: patients who underwent surgery within 18 days and patients who underwent surgery later than 18 days after SEMS placement. Of the 112 patients, 20 patients underwent emergency surgery due to failure of the stent placement. These patients were excluded from the analysis. A logistic regression analysis was performed. We found a significant increased risk of recurrence in the group with more than 18 days from stent placement to elective surgery (OR 5.1 [1.6–15.8], $p = 0.005$). See Table 3. Furthermore, we performed the analysis as an "intention-to-treat" model including patients undergoing emergency surgery because of complications due to stent placement. In this analysis, we also found a significant increased risk of recurrence in the group with more than 18 days from stent placement to surgery (OR 2.6 [1.1–6.5], $p = 0.037$). Additionally, we found a significantly lower risk of recurrence related to increasing age at stent placement (OR 0.96 [0.91–1.00], $p = 0.049$). See Table 4.

Table 2 Survival and recurrence rate

	$n = 112$
30-day survival	106 (95)
1-year survival	101 (90)
Survival at follow-up	78 (70)
Recurrence rate	41 (37)
Metastasis location	
Lung	13 (12)
Liver	17 (15)
Local	19 (17)
Other	4 (3)
Postoperative complications (Clavien-Dindo)	
1	4 (4)
2	10 (9)
3a	4 (4)
3b	18 (16)
4a	3 (3)
4b	2 (2)
5	2 (2)
Complication to stent	
Migration	10 (9)
Perforation	10 (9)
Days from stent placement to resection, median (IQR)[a]	18 (23)

Data are expressed as *n* (%) unless indicated otherwise

[a] Time from stent placement to resection, if relevant

Table 3 Multiple logistic regression analysis—time to resection (<18 vs ≥18 days) and the risk of metastasis, controlled with age, gender, T stage, and postoperative chemotherapy

Covariates	Odds ratio (95% confidence limits)	*p*
Male gender	1.3 (0.5–3.6)	0.569
Age	0.96 (0.9–1.0)	0.069
Time to resection (≥18 days)	5.1 (1.6–15.8)	0.005
Tumor grade	1.6 (0.5–4.5)	0.413
Chemotherapy	1.6 (0.6–4.8)	0.362

Discussion

This study found a relatively high recurrence rate of 37%, primarily local recurrences followed by metastases in the lungs and liver, in patients undergoing SEMS placement as bridge to surgery. Our analysis showed a significantly higher recurrence rate related to increasing time from SEMS placement to surgery. Larger studies are needed to verify the results

Table 4 Intention-to-treat model multiple logistic regression analysis—time to resection (<18 vs ≥18 days) and the risk of metastasis, controlled with age, gender, T stage, and postoperative chemotherapy

Covariates	Odds ratio (95% confidence limits)	*p*
Male gender	1.6 (0.7–3.9)	0.288
Age	0.96 (0.91–1.00)	0.049
Time to resection (≥18 days)	2.6 (1.1–6.5)	0.037
Tumor grade	1.8 (0.7–4.6)	0.195
Chemotherapy	1.7 (0.7–4.3)	0.282

found in this study. Furthermore, it is relevant to note that 18% needed an emergency surgery due to a stent-related complication, primarily perforation or migration.

Recent studies have failed to show beneficial effects of stenting as bridge to surgery over emergency surgery [12–14]. A number of meta-analyses support these findings [4, 15, 16]. In the past few years, long-term oncologic outcomes have been discussed. In 2014, a study ended prematurely, as they found a risk of recurrence associated with stent placement for malignant colonic obstruction [17]. Additionally, in 2013, one study reported increased local recurrence rate after SEMS placement compared with emergency surgery [6]. A number of reasons for these findings have been suggested. Several studies have demonstrated increased histopathological changes in patients undergoing SEMS placement compared with emergency surgery [18–20]. These studies reported higher rates of perineural invasion, inflammation, lymph node invasion, ulceration at or near the tumor, and necrosis. Additionally, tumor cell dissemination following SEMS placement has been reported [21].

The high recurrence rate in our study supports the findings of other studies. Efforts were made to minimize the limitations of this study, primarily due to the retrospective design. However, selection bias among others cannot be ruled out. Our study should be interpreted with caution. Larger prospective studies are needed to confirm our findings.

In conclusion, our study found a relatively high recurrence rate after SEMS placement as bridge to surgery for malignant colonic obstruction. Furthermore, we found a higher risk of recurrence associated with increased time from SEMS placement to elective surgery.

Compliance with ethical standards The current study was approved by the Danish Data Protection Agency (REG-74-2015).

Conflict of interest The authors declare that they have no conflict of interest.

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