Time interval between self-expandable metal stent placement or creation of a decompressing stoma and elective resection of left-sided obstructive colon cancer

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ABSTRACT

Background The optimal timing of resection after decompression of left-sided obstructive colon cancer is unknown. Revised expert-based guideline recommendations have shifted from an interval of 5 – 10 days to approximately 2 weeks following self-expandable metal stent (SEMS) placement, and recommendations after decompressing stoma are lacking. We aimed to evaluate the recommended bridging intervals after SEMS and explore the timing of resection after decompressing stoma.

Methods This nationwide study included patients registered between 2009 and 2016 in the prospective, mandatory Dutch ColoRectal Audit. Additional data were collected through patient records in 75 hospitals. Only patients who underwent either SEMS placement or decompressing stoma as a bridge to surgery were selected. Technical SEMS failure and unsuccessful decompression within 48 hours were exclusion criteria.

Results 510 patients were included (182 SEMS, 328 decompressing stoma). Median bridging interval was 23 days (interquartile range [IQR] 13 – 31) for SEMS and 36 days (IQR 22 – 65) for decompressing stoma. Following SEMS placement, no significant differences in post-resection complications, hospital stay, or laparoscopic resections were observed with resection after 11 – 17 days compared with 5 – 10 days. Of SEMS-related complications, 48 % occurred in patients operated on beyond 17 days. Compared with resection within 14 days, an interval of 14 – 28 days following decompressing stoma resulted in significantly more laparoscopic resections, more primary anastomoses, and shorter hospital stays. No impact of bridging interval on mortality, disease-free survival, or overall survival was demonstrated.

Conclusions Based on an overview of the data with balancing of surgical outcomes and timing of adverse events, a bridging interval of approximately 2 weeks seems appropriate after SEMS placement, while waiting 2 – 4 weeks after decompressing stoma further optimizes surgical conditions for laparoscopic resection with restoration of bowel continuity.

Introduction

Emergency major general surgery is generally known for its high mortality and morbidity rates [1, 2]. Segmental colectomy is one of the seven procedures that collectively contribute to 80 % of the mortality, morbidity, and costs of emergency general surgery [3]. For patients with left-sided obstructive colon cancer (LSOCC), emergency colectomy might be avoided by choosing a bridge to elective surgery (BTS) strategy.

Postponing resection of LSOCC can be achieved by either colonic self-expandable metal stent (SEMS) placement or the construction of a decompressing stoma [4 – 6]. After initial relief of the obstruction, time is created for there to be an improvement in the patient's condition, for accurate preoperative staging, and to compile an experienced surgical team. Furthermore, the distended bowel proximal to the tumor returns to its normal caliber with optimized surgical conditions to restore bowel continuity.

The optimal timing of resection following a decompressing intervention remains unclear. It is generally assumed that improvement in the patient's clinical and intestinal condition takes a few weeks [7]. On the other hand, concerns have been raised regarding the risk of SEMS-related perforation if the bridging interval is prolonged. In their guideline of 2014, the European Society of Gastrointestinal Endoscopy (ESGE) suggested a time interval of 5 – 10 days from SEMS placement until elective resection [8]. The recent update suggests an interval of approximately 2 weeks, but still as a weak recommendation, this being largely based on expert opinion [9]. We are not aware of any relevant literature or guideline recommendations regarding the bridging interval following a decompressing stoma.

Analysis of patients with LSOCC treated between 2009 and 2016 in the Netherlands revealed substantial variability in bridging intervals for both SEMSs and decompressing stomas [10], sufficient to determine whether the bridging interval affected outcomes such as resection-related complications, short-term mortality, and survival [11]. Therefore, the aim of the current study was to evaluate the recommended bridging intervals after SEMS placement and to explore the bridging interval after decompressing stoma within the Dutch nationwide cohort of LSOCC, with 90-day post-resection complications as the primary outcome measure.

Methods

Study design and patient selection

A nationwide, population-based study was performed by the Dutch Snapshot Research Group (DSRG), as described previously [10]. Each hospital in the Netherlands (n = 77) was requested to extend baseline and short-term outcome data prospectively collected in the Dutch ColoRectal Audit (DCRA) with supplementary diagnostic, procedural, and intermediate-term data by reviewing individual patient files, using a web-based tool that meets Dutch privacy regulations, followed by a data verification process. This study was approved by the Institutional Review Board of the Academic Medical Center in Amsterdam, The Netherlands. Informed consent was not required owing to the retrospective design of the study and the use of anonymized data.

For the current study, the eligibility criteria included registered patients between 2009 and 2016 who had: (1) a colonic obstruction causing symptoms including a distended abdomen, nausea, and/or vomiting, (2) with radiological signs of obstruction either on computed tomography (CT) or plain radiograph, (3) caused by a histologically proven tumor, (4) located

in the distal colon (defined as the sigmoid colon, descending colon, or splenic flexure), (5) that was initially treated with either a SEMS or decompressing stoma as a BTS, (6) with curative treatment intent. Exclusion criteria were: (1) signs of bowel perforation on CT at baseline; (2) technically unsuccessful bridging intervention; and (3) clinically unsuccessful bridging intervention (defined as the absence of symptom relief within 48 hours after the initial intervention).

Procedural characteristics and outcome measures

Procedural characteristics were the proportions of patients being discharged during the bridging interval, undergoing intentional laparoscopic approach, and with a primary anastomosis or a stoma in situ directly after tumor resection.

The primary outcome parameter was the proportion of resection-related complications within 90 days after resection of the primary tumor. The SEMS-related complication rate following technically and clinically successful SEMS placement was added as a primary outcome parameter for the SEMS subgroup. Secondary outcome measures were the 90-day post-resection mortality rate, hospital stay after resection, 3-year disease-free survival, and 3-year overall survival.

Statistical analysis

Cumulative incidence curves with bridging interval on the *x*-axis were made for selected variables: 90-day post-resection complications, SEMS-related complications, laparoscopic approach, and primary anastomosis. Cumulative incidence curves were made by determining the number of patients that had already been operated on, and how many of these had had an event, according to the outcome variable concerned, for each day since the bridging intervention. The number of patients with an event was then divided by the total number of patients that had been at risk until a specific time interval, and these proportions were plotted with the time interval in days on the *x*-axis and the outcome variable on the *y*-axis.

The procedural characteristics and outcome measures of the SEMS and decompressing stoma groups were determined for different bridging intervals. Bridging intervals that were analyzed for the SEMS group were: 5 – 10 days (2014 ESGE guideline) [8], 11 – 17 days (2020 ESGE recommendation of approximately 2 weeks) [9], and > 17 days. Bridging intervals for decompressing stoma were chosen based on clinical relevance in the absence of existing guideline recommendations that could be validated: < 14 days (early, same admission), 14 – 28 days (elective, more recovery time), and > 28 days (delayed, possibility of neoadjuvant treatment).

Continuous variables were tested for normality using the Kolmogorov – Smirnoff test. Normally distributed continuous variables were reported as mean (standard deviation [SD]) and hypotheses regarding these variables were tested with the Student's *t* test for comparison of two groups or the one-way ANOVA test for more than two groups. Non-normally distributed variables were reported as medians (interquartile range [IQR]), with hypotheses being tested with the Mann – Whitney *U* test for comparison of two groups or the Kruskal Wallis test for more than two groups. Categorical variables were reported as percentages and hypotheses were tested with the chi-squared or Fisher's exact test. Differences regarding disease-free and overall survival were assessed using the log-rank test.

A two-sided *P* value < 0.05 was considered statistically significant. Correction for multiple testing was performed when comparing groups of intervals by adhering to a two-sided *P* value < 0.025 as statistically significant. All analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, New York, USA).

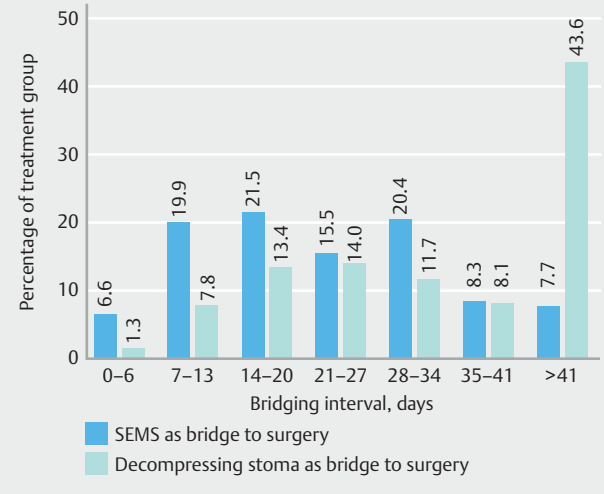
Results

Baseline characteristics

A total of 75 of 77 hospitals provided supplementary data on the patients who were originally identified from the DCRA, with 3879 of 4216 potentially eligible patients (92.0 %) identified. **Fig. 1s** (see online-only Supplementary Material) shows the number of patients who were excluded for each reason. A total of 510 patients who underwent a BTS approach remained for final analyses, of whom 182 underwent SEMS placement (35.7 %) and 328 underwent construction of a decompressing stoma (64.3 %).

Baseline characteristics for SEMS and decompressing stoma patients are displayed in ▶ **Table 1**. The median bridging interval to elective resection was 23 days (IQR 13 – 31) for SEMS and 36 days (IQR 22 – 65) for decompressing stoma patients. The percentage of patients undergoing surgery after different bridging intervals is displayed for the SEMS and decompressing stoma groups in ▶ **Fig. 1**. Long bridging intervals (> 6 weeks) were mainly observed in the decompressing stoma group (43.6 % of decompressing stoma patients). Of decompressing stoma patients with an interval > 6 weeks, 45 (35.2 %) received neoadjuvant therapy (not shown).

During the bridging interval, 11 SEMS (6.7 %) and 23 decompressing stoma patients (7.7 %) were parenterally fed, while 14 SEMS (8.5 %) and 12 decompressing stoma patients (4.1 %) re-



▶ **Fig. 1** Percentage of patients in each group undergoing surgery after the different bridging intervals.

▶ **Table 1** Baseline characteristics, procedural indicators, and treatment outcomes.

	Bridge to elective surgery	
	SEMS (n = 182)	Decompressing stoma (n = 328)
Male sex, n/N (%)	107/182 (58.8)	193/328 (58.8)
Median age (IQR), years	72.0 (63.8 – 81.0)	68.0 (59.0 – 76.8)
Mean BMI (SD), kg/m2	25.7 (4.5)	25.3 (4.2)
ASA score, n/N (%)		
▪ ASA 1	40/178 (22.5)	44/328 (13.4)
▪ ASA 2	98/178 (55.1)	212/328 (64.6)
▪ ASA 3	37/178 (20.8)	67/328 (20.4)
▪ ASA 4	3/178 (1.7)	5/328 (1.5)
Comorbidity, n (%)	128/180 (71.1)	232/328 (70.7)
Previous abdominal surgery, n/N (%)	39/179 (21.8)	123/328 (37.5)
Tumor localization, n/N (%)		
▪ Splenic flexure	11/182 (6.0)	52/328 (15.9)
▪ Descending colon	42/182 (23.1)	54/328 (16.5)
▪ Sigmoid	129/182 (70.9)	222328 (67.7)
Median interval from initial therapy to resection (IQR), days	23.0 (13.0 – 31.0)	36.0 (22.0 – 64.5)
Parenteral feeding during bridging interval, n/N (%)	11/163 (6.7)	23/300 (7.7)
Enteral tube feeding during bridging interval, n/N (%)	14/165 (8.5)	12/296 (4.1)
Neoadjuvant therapy during bridging interval, n/n (%)	3/182 (1.6)	52/328 (15.9)
▪ Systemic therapy	1/176 (0.6)	49/317 (15.5)
▪ Radiation therapy	2/176 (1.1)	20/318 (6.3)
Discharge from hospital during bridging interval, n/N (%)	134/172 (77.9)	278/312 (89.1)
Type of resection, n/N (%)		
▪ Sigmoid resection	113/182 (62.1)	201/328 (61.3)
▪ Left hemicolectomy	64/182 (35.2)	99/328 (30.2)
▪ Subtotal colectomy	3/182 (1.6)	19/328 (5.8)
▪ Extended left hemicolectomy	1/182 (0.5)	7/328 (2.1)
▪ Transverse colectomy	1/182 (0.5)	2/328 (0.6)
Laparoscopic resection, n/N (%)	91/179 (50.8)	161/327 (49.2)
Converted laparoscopic resection, n/N (%)	19/64 (29.7)	27/157 (17.2)
Primary anastomosis, n/N (%)	152/181 (84.0)	280/327 (85.6)
Stoma directly after resection, n/N (%)	37/175 (21.1)	214/326 (65.6)
Resection-related complications <90 days, n/N (%)	51/178 (28.7)	81/323 (25.1)
▪ Anastomotic leakage	16/152 (10.5)	15/280 (5.4)
▪ Intra-abdominal abscess	10/182 (5.5)	11/326 (3.4)
▪ Fascial dehiscence	11/177 (6.2)	5/311 (1.6)
▪ Wound infection	13/176 (7.4)	33/315 (10.5)
▪ Ileus	7/176 (4.0)	10/313 (3.2)
▪ Gastroparesis	7/176 (4.0)	6/312 (1.9)
▪ Bleeding	2/176 (1.1)	3/313 (1.0)
▪ Abdominal wall abscess	3/176 (1.7)	2/311 (0.6)
Median post-resection hospital stay (IQR), days	7.0 (5.0 – 12.0)	7.0 (5.0 – 10.0)
90-day mortality, n/N (%)	10/182 (5.5)	8/328 (2.4)
3-year disease free survival, %	63.0	61.3
▪ Cumulative events at 36 months	58	95
▪ Patients at risk at 36 months	87	96
3-year overall survival, %	73.0	76.2
▪ Cumulative events at 36 months	42	53
▪ Patients at risk at 36 months	98	110

ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; SD, standard deviation; SEMS, self-expandable metal stent.

ceived enteral tube feeding. Neoadjuvant therapy during the bridging interval was applied in 3 SEMS (1.6 %) and 52 decompressing stoma patients (15.9 %), mainly consisting of systemic therapy. The median follow-up was 43.5 months (IQR 17.0 – 66.0) for the SEMS group and 25.0 months (IQR 14.8 – 46.3) for the decompressing stoma group.

Procedural and outcome parameters

Cumulative incidence curves revealed peaks with higher rates of 90-day post-resection complications if resection was performed within 2 weeks of colonic decompression, especially after decompressing stoma. These rates stabilized at a lower level from a bridging interval of 15 days onwards (▶ **Fig. 2a**).

After the exclusion of patients who underwent emergency resection at < 48 hours because of SEMS failure, 23 patients developed SEMS-related complications. Overall, SEMS-related perforations occurred in 12 patients (12 / 169 [7.1 %]; missing data in 13 patients), including three with clinically overt perforations, eight with SEMS perforations that were intraoperatively identified during resection, and one with a perforation that was found histopathologically. Visual evaluation of the graphical data regarding SEMS-related complications showed a peak for a bridging interval of about 1 week, with stabilization at a lower level for bridging intervals of more than 4 weeks (▶ **Fig. 2b**). The median time from SEMS placement to SEMS-related complication was 7.0 days (IQR 5.0 – 20.0).

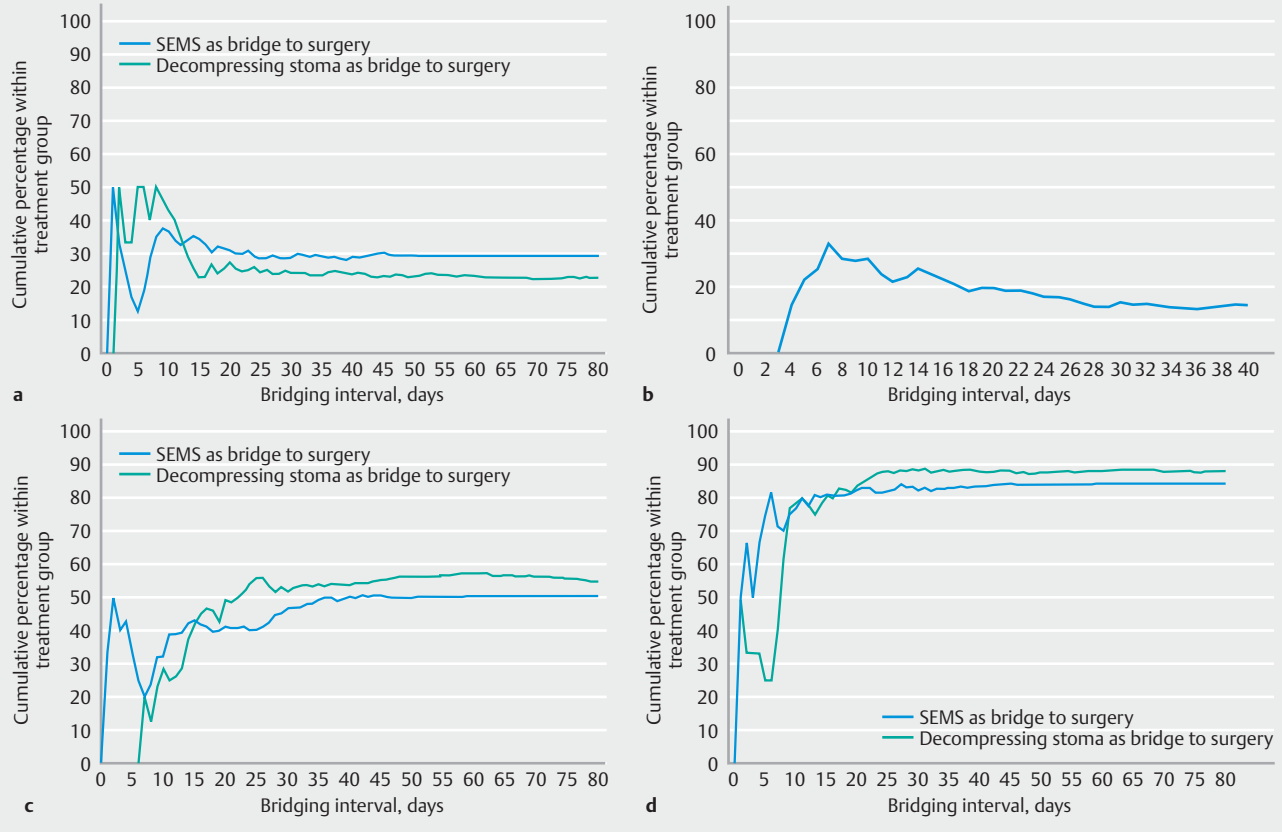
Cumulative incidence curves of laparoscopic approach revealed an increase with increasing bridging interval up to 5 weeks after decompressing stoma and stabilization thereafter, while this influence of bridging interval was less clear after SEMS placement (▶ **Fig. 2c**). Similarly, primary anastomoses were increasingly performed with longer bridging intervals, with stabilization from 3 to 4 weeks onwards, which was more pronounced after decompressing stoma (▶ **Fig. 2d**).

Comparisons of bridging intervals

The different procedural and outcome parameters of the SEMS and decompressing stoma groups are displayed in ▶ **Table 2** for the different prespecified bridging intervals, depending on the type of intervention. These outcome parameters were also calculated for 1-week increments of the bridging interval until 34 days and for the remaining group who underwent resection after > 34 days, thereby providing detailed data that enable other explorative analyses or pooling of data (**Table 1s**).

SEMS group

The 90-day post-resection complication rate was lower for a bridging interval of 11 – 17 days compared with 5 – 10 days, although this did not reach statistical significance (25.0 % vs.



▶ **Fig. 2** Cumulative percentage graphs of patients who had, with increasing bridging intervals: **a** a resection-related complication; **b** a self-expandable metal stent (SEMS)-related complication; **c** a laparoscopically performed resection; **d** a primary anastomosis.

▶ **Table 2** Procedural characteristics and treatment outcomes for SEMS and decompressing stoma as a bridge to elective surgery, stratified for different bridging intervals.

Self-expandable metal stent (SEMS)							
	Bridging interval, days			*P* value			
	5 – 10 (n = 24)	11 – 17 (n = 38)	> 17 (n = 112)	Overall	5 – 10 vs. 11 – 17	11 – 17 vs. > 17	5 – 10 vs. > 17
Procedural characteristics							
Discharge from hospital during bridging interval, n/N (%)	6/22 (27.3)	31/37 (83.8)	97/105 (92.4)	< 0.001	< 0.001	0.20	< 0.001
Laparoscopic resection, n/N (%)	7/24 (29.2)	18/37 (48.6)	62/110 (56.4)	0.052	0.13	0.42	0.02
Conversion of laparoscopic resection, n/N (%)	2/4 (50.0)[1]	5/11 (45.5)[2]	11/46 (23.9)[3]	0.21	> 0.99	0.26	0.28
Primary anastomosis, n/N (%)	19/24 (79.2)	32/38 (84.2)	96/112 (85.7)	0.72	0.74	0.82	0.53
Stoma in situ directly after resection, n/N (%)	9/23 (39.1)	6/36 (16.7)	19/109 (17.4)	0.07	0.053	0.92	0.046
Outcome variables							
Resection-related complications < 90 days, n/N (%)	10/24 (41.7)	9/36 (25.0)	31/111 (27.9)	0.33	0.17	0.73	0.18
SEMS-related complication[4], n/N (%)	7/21 (33.3)	5/35 (14.3)	11/105 (10.5)	0.02	0.11	0.55	0.01
▪ Clinically overt perforation	1	1	1				
▪ Perforation identified during resection	2	2	4				
▪ Perforation identified during pathological examination	1	0	0				
▪ Migration	2	1	1				
▪ Obstruction	1	1	6				
▪ Rectal bleeding	0	0	1				
▪ Rectal/abdominal pain	1	0	2				
Median post-resection hospital stay (IQR), days	8.0 (5.0 – 15.3)	6.0 (4.0 – 8.0)	7.0 (5.0 – 12.0)	0.25	0.12	0.25	0.30
Adjuvant chemotherapy, n/N (%)	8/23 (34.8)	19/38 (50.0)	39/112 (34.8)	0.24	0.25	0.10	> 0.99
90-day mortality, n/N (%)	1/24 (4.2)	1/38 (2.6)	8/112 (7.1)	0.55	> 0.99	0.45	> 0.99
3-year disease free survival, %[5]	49.7	78.1	62.0	0.31	0.14	0.19	0.60
3-year overall survival, %[5]	63.2	80.7	72.8	0.48	0.27	0.27	0.75
Decompressing stoma							
	Bridging interval, days			*P* value			
	< 14 (n = 28)	14 – 28 (n = 92)	> 28 (n = 187)	Overall	< 14 vs. 14 – 28	14 – 28 vs. > 28	< 14 vs. > 28
Procedural characteristics							
Discharge from hospital during bridging interval, n/N (%)	10/27 (37.0)	77/90 (85.6)	178/181 (98.3)	< 0.001	< 0.001	< 0.001	< 0.001
Laparoscopic resection, n/N (%)	8/28 (28.6)	58/92 (63.0)	85/186 (45.7)	0.002	0.001	0.006	0.09
Conversion of laparoscopic resection, n/N (%)	1/7 (14.3)	12/58 (20.7)	13/82 (15.9)	0.81	> 0.99	0.46	> 0.99
Primary anastomosis, n/N (%)	21/28 (75.0)	84/91 (92.3)	158/187 (84.5)	0.047	0.01	0.07	0.27
Stoma in situ directly after resection, n/N (%)	19/27 (70.4)	64/92 (69.6)	119/186 (64.0)	0.58	0.94	0.36	0.52

Decompressing stoma (Continuation)							
Outcome variables							
Resection-related complications < 90 days, n/N (%)	8/27 (29.6)	20/90 (22.2)	48/186 (25.8)	0.69	0.43	0.52	0.67
Median post-resection hospital stay (IQR), days	10.0 (6.0 – 18.8)	7.0 (4.8 – 9.3)	7.0 (5.0 – 10.0)	0.07	0.03	0.37	0.06
Adjuvant chemotherapy, n/N (%)	11/28 (39.3)	42/89 (47.2)	69/185 (37.3)	0.29	0.46	0.12	0.84
90-day mortality, n/N (%)	2/28 (7.1)	2/92 (2.2)	4/187 (2.1)	0.26	0.23	> 0.99	0.18
3-year disease free survival, %[5]	67.1	64.0	59.6	0.87	0.67	0.60	0.91
3-year overall survival, %[5]	71.0	80.3	75.4	0.68	0.57	0.39	0.92

IQR, interquartile range; NA, not applicable.
[1] Data missing in 3 patients.
[2] Data missing in 7 patients.
[3] Data missing in 16 patients.
[4] More than one complication per patient could be registered.
[5] Log-rank test.

41.7 %; $P = 0.17$) (▶ **Table 2**). The post-resection complication rate did not significantly differ between the cutoff values of 11 – 17 and > 17 days. A trend towards shorter post-resection hospital stay was observed for a bridging interval of 11 – 17 days vs. 5 – 10 days (6 vs. 8 days; $P = 0.12$). Of the 12 SEMS-related perforations, five were observed in patients being operated on beyond 17 days, as were 6/8 SEMS obstructions. Of all 23 patients with SEMS-related complications, 11 (48 %) underwent resection with an interval of > 17 days.

The proportion of laparoscopic surgery increased with longer bridging intervals (29.2 % for 5 – 10 days; 48.6 % for 11 – 17 days; 56.4 % for > 17 days), although this did not reach statistical significance. Fewer patients had a stoma in situ directly after resection following a bridging interval of 11 – 17 days compared with 5 – 10 days (16.7 % vs. 39.1 %; $P = 0.053$). No significant differences were observed for 90-day mortality, 3-year disease-free survival, or 3-year overall survival.

Decompressing stoma group

No significant differences in post-resection complication rates were observed for any of the cutoff values (▶ **Table 2**). Resections were more often performed laparoscopically when waiting 14 – 28 days compared with < 14 days (63.0 % vs. 28.6 %; $P = 0.001$). The laparoscopy rate decreased to 45.7 % in patients who underwent resection beyond 28 days ($P = 0.006$). Resection 14 – 28 days after initial decompressing stoma resulted in significantly more primary anastomoses (92.3 % vs. 75.0 %; $P = 0.01$). Post-resection hospital stay was shorter if resection was performed in the period of 14 – 28 days after decompression when compared with resection within 14 days (7 vs. 10 days; $P = 0.03$), although this was not statistically significant after correction for multiple testing ($P > 0.025$). No significant differences were observed for 90-day mortality, 3-year disease-free survival, or 3-year overall survival.

Discussion

This large population-based cohort study evaluated ESGE guideline recommendations regarding bridging interval following colonic stenting and explored clinically relevant bridging intervals after decompressing stoma. Following SEMS, fewer post-resection complications, shorter post-resection hospital stay, and more laparoscopic resections were observed with tumor resection performed 11 – 17 days after initial decompression compared with resection after 5 – 10 days, although not reaching statistical significance. Almost half of the SEMS-related complications, including five perforations and six obstructions, occurred in patients who underwent resection beyond 17 days.

Bridging intervals following decompressing stoma were generally longer than after SEMS (median 36 vs. 23 days), and 15 % of decompressing stoma patients underwent neoadjuvant treatment for locally advanced colon cancer with delayed resection. If compared with resection within 14 days, a bridging interval of 14 – 28 days following decompressing stoma resulted in significantly more laparoscopic resections, more primary anastomoses, and shorter post-resection hospital stays. No impact of bridging intervals on postoperative mortality, disease-free survival, or overall survival could be demonstrated.

Literature on the bridging interval following SEMS placement or creation of a decompressing stoma is scarce. A single institutional series by Matsuda et al. [12] analyzed 47 patients with a SEMS followed by resection (two patients with stent migration were excluded). Eight patients developed post-resection complications with a Clavien – Dindo score ≥ 2 [13]. For resection performed at ≤ 15 days, 7/19 patients (37 %) developed postoperative complications, compared with 1/28 patients (4 %) who underwent surgery beyond 15 days (odds ratio [OR] 13.0; 95 % confidence interval [CI] 1.01 – 167.0). These findings are in line with the present study, although the effect size and significance levels are fundamentally different.

In a comparative analysis of 43 patients who underwent SEMS placement followed by elective resection, Lee et al. [14] found a significant association between bridging interval and anastomotic leakage: 3/15 patients with an interval of 1 – 9 days and 0/28 patients with an interval ≥ 10 days. In the Stent-in II trial [15], a leak rate of 5/21 patients (24 %) was observed with a recommended bridging interval in the study protocol between 5 and 14 days, and the authors speculated that a longer wait could have improved results. The only contradictory finding in the literature is by Ho et al. [16], who reported on only 14 patients who had successful SEMS placement with a median of 10 days until elective resection. Without any supporting data, they state that an interval between 9 and 14 days might be optimal with a higher risk of dense fibrotic adhesions at the level of the stent after 14 days of waiting, which might complicate surgery.

One study specifically analyzed the association between bridging interval and oncological outcome [17]. In this study, 20/112 patients (18 %) had stent-related complications requiring emergency surgery, consisting of perforation and migration in 10 patients each. The overall recurrence rate was 37 %. Using the median bridging interval of 18 days as a cutoff, a longer bridging interval was significantly associated with overall tumor recurrence, with an OR of 2.6 (95 %CI 1.1 – 6.5) for the intention-to-treat population and an OR of 5.1 (95 %CI 1.6 – 15.8) after correction for age, sex, T-stage, and adjuvant chemotherapy. This is in contrast to the present study, in which no differences in disease-free survival were observed among the different bridging interval groups.

Regarding the decompressing stoma group, similar analyses are lacking in the current literature. Jiang et al. [18] reported on 90 patients with a decompressing stoma as a BTS, with a mean interval of 16 days (range 3 – 73 days). In the randomized trial by Kronborg et al. [19], the study protocol described a 2-week bridging interval between decompressing stoma and subsequent resection, but they did not provide data on the bridging intervals. A recent single-center cohort study described a median 25 days (IQR 17 – 47) between colostomy and resection among 85 patients [4]. Oistamo et al. [20] described the longest bridging interval, with a mean of 37 days in a group of 20 patients. None of these studies on decompressing stoma as a BTS included any analysis regarding the association between bridging interval and outcome.

Physicians likely had specific reasons for each particular bridging interval based on their patient's condition, age, tumor stage, and other logistical aspects, resulting in allocation bias. Only a randomized controlled trial (RCT) would solve this methodological issue. In patients with LSOCC, RCTs are apparently difficult to conduct, as illustrated by the published literature to date. Clear preferences of doctors and patients regarding the type of bridging technique and certain bridging intervals would likely result in limited protocol adherence. RCTs in this setting are often characterized by slow accrual and restricted external validity as a result of strict and narrow inclusion criteria.

The findings of this study, together with the scarcity of available evidence from the literature, suggest that a 2-week gap to definitive surgery is recommended in order for patients to benefit from a decompressing intervention, and a prolonged waiting period seems not to be associated with higher oncological risks. Improvements in a patient's general and surgical condition need some time, as illustrated by ▶ **Fig. 2**. This is reflected by the continuing increase in the proportion of primary anastomoses up to a 4-week bridging interval, especially after decompressing stoma. The main limitation for longer waiting concerns SEMS-related complications. Among the SEMS-related complications, perforation is actually the most severe one that should guide clinical decision-making. Stent obstruction may be endoscopically managed [12], and stent migration might prohibit further waiting, but without the worsening oncological outcome.

After successful SEMS placement, a 2-week interval probably results in the optimal balance between better surgical condition on the one hand and prevention of SEMS-related complications on the other hand. By following an approximately 2-week interval, which is according to the most recent update of the ESGE guideline [9], five SEMS-related perforations may have been prevented, along with prevention of other complications such as obstruction. Furthermore, the largest gain in minimally invasive approach and bowel continuity has likely been reached by that time.

After creation of a decompressing stoma, there is less urgency to perform the resection, and an interval of 2 – 4 weeks appeared to be associated with clinical benefits in terms of laparoscopic approach, bowel continuity, and hospital stay. Striving for more laparoscopic resections is worthwhile, not only because of enhanced recovery, but also because of long-term advantages, such as fewer incisional hernias and adhesion-related small-bowel obstruction compared with open resections [21 – 23]. Of course, neoadjuvant therapy would dictate the length of the bridging interval in appropriate patients, and such patients with locally advanced disease are less likely to undergo laparoscopy.

The limitations of the current study include the retrospective study design with its inherent methodological shortcomings. Arguments for choosing a specific bridging interval were unknown. Allocation bias might have affected the results observed in the current study. Furthermore, the DCRA includes only patients who underwent tumor resection. Patients who died during the bridging interval were therefore not included in the current study, which might have caused overly optimistic results. As few [4] to no deaths [24] during the bridging interval have been reported so far for decompressing stoma and SEMS placement in the curative setting, we do not expect a large influence on our results. Additionally, we excluded patients who did not achieve clinical success within 48 hours after bridging, a timeframe that was chosen arbitrarily. As a result, the group of patients with an interval < 1 week might still include patients with unsuccessful colonic decompression. Regarding testing for statistical significance, one should keep in mind the potential type 1 and 2 errors, which underlines the need for careful interpretation. Finally, despite some data on parenteral or enteral tube feeding being available, little was known on prehabilitation measures and improvement of patients' clinical condition, such as gain in body weight, during the bridging interval.

In conclusion, this large national cohort of patients with LSOCC shows that surgical conditions for elective resection improved with intervals of up to 4 weeks after SEMS placement or stoma creation, as reflected by increasing rates of laparoscopic resection and primary anastomosis. An optimized balance between SEMS-related complications and recovery of the patient with optimized surgical conditions is probably achieved by scheduling the resection after approximately 2 weeks following successful SEMS placement. After creation of a decompressing stoma, a bridging interval of 2 – 4 weeks is suggested.

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Competing interests

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References

[1] Havens JM, Peetz AB, Do WS et al. The excess morbidity and mortality of emergency general surgery. J Trauma Acute Care Surg 2015; 78: 306–311

[2] Ball CG, Murphy P, Verhoeff K et al. A 30-day prospective audit of all inpatient complications following acute care surgery: How well do we really perform? Can J Surg 2020; 63: E150–E154

[3] Scott JW, Olufajo OA, Brat GA et al. Use of national burden to define operative emergency general surgery. JAMA Surg 2016; 151: e160480

[4] Amelung FJ, Mulder CL, Broeders IA et al. Efficacy of loop colostomy construction for acute left-sided colonic obstructions: a cohort analysis. Int J Colorectal Dis 2017; 32: 383–390

[5] Veld JV, Amelung FJ, Borstlap WAA et al. Comparison of decompressing stoma vs stent as a bridge to surgery for left-sided obstructive colon cancer. JAMA Surg 2020; 155: 206–215

[6] Amelung FJ, Ter Borg F, Consten EC et al. Deviating colostomy construction versus stent placement as bridge to surgery for malignant left-sided colonic obstruction. Surg Endosc 2016; 30: 5345–5355

[7] Gillis C, Buhler K, Bresee L et al. Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. Gastroenterology 2018; 155: 391–410 e394

[8] van Hooft JE, van Halsema EE, Vanbiervliet G et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2014; 46: 990–1053

[9] van Hooft JE, Veld JV, Arnold D et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2020. Endoscopy 2020; 52: 389–407

[10] Veld JV, Amelung FJ, Borstlap WAA et al. Changes in management of left-sided obstructive colon cancer: national practice and guideline implementation. J Natl Compr Canc Netw 2019; 17: 1512–1520

[11] Wong SL, Ji H, Hollenbeck BK et al. Hospital lymph node examination rates and survival after resection for colon cancer. JAMA 2007; 298: 2149–2154

[12] Matsuda A, Miyashita M, Matsumoto S et al. Optimal interval from placement of a self-expandable metallic stent to surgery in patients with malignant large bowel obstruction: a preliminary study. Surg Laparosc Endosc Percutan Tech 2018; 28: 239–244

[13] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205–213

[14] Lee GJ, Kim HJ, Baek JH et al. Comparison of short-term outcomes after elective surgery following endoscopic stent insertion and emergency surgery for obstructive colorectal cancer. Int J Surg 2013; 11: 442–446

[15] van Hooft JE, Bemelman WA, Oldenburg B et al. Colonic stenting versus emergency surgery for acute left-sided malignant colonic obstruction: a multicentre randomised trial. Lancet Oncol 2011; 12: 344–352

[16] Ho KS, Quah HM, Lim JF et al. Endoscopic stenting and elective surgery versus emergency surgery for left-sided malignant colonic obstruction: a prospective randomized trial. Int J Colorectal Dis 2012; 27: 355–362

[17] Broholm M, Kobborg M, Frostberg E et al. Delay of surgery after stent placement for resectable malignant colorectal obstruction is associated with higher risk of recurrence. Int J Colorectal Dis 2017; 32: 513–516

[18] Jiang JK, Lan YT, Lin TC et al. Primary vs. delayed resection for obstructive left-sided colorectal cancer: impact of surgery on patient outcome. Dis Colon Rectum 2008; 51: 306–311

[19] Kronborg O. Acute obstruction from tumour in the left colon without spread. A randomized trial of emergency colostomy versus resection. . Int J Colorectal Dis 1995; 10: 1–5

[20] Oistamo E, Hjern F, Blomqvist L et al. Emergency management with resection versus proximal stoma or stent treatment and planned resection in malignant left-sided colon obstruction. World J Surg Oncol 2016; 14: 232

[21] Aquina CT, Probst CP, Becerra AZ et al. Missed opportunity: laparoscopic colorectal resection is associated with lower incidence of small bowel obstruction compared to an open approach. Ann Surg 2016; 264: 127–134

[22] Klaristenfeld DD, McLemore EC, Li BH et al. Significant reduction in the incidence of small bowel obstruction and ventral hernia after laparoscopic compared to open segmental colorectal resection. Langenbecks Arch Surg 2015; 400: 505–512

[23] Udayasiri DK, Skandarajah A, Hayes IP. Laparoscopic compared with open resection for colorectal cancer and long-term incidence of adhesional intestinal obstruction and incisional hernia: a systematic review and meta-analysis. Dis Colon Rectum 2020; 63: 101–112

[24] Arezzo A, Passera R, Lo Secco G et al. Stent as bridge to surgery for left-sided malignant colonic obstruction reduces adverse events and stoma rate compared with emergency surgery: results of a systematic review and meta-analysis of randomized controlled trials. Gastrointest Endosc 2017; 86: 416–426