


The prognostic impact of bowel perforation following self-expanding metal stent as a bridge to surgery in colorectal cancer obstruction

Tue Højslev Avlund¹  · Rune Erichsen^{1,2} · Sissel Ravn¹ · Zydrunas Ciplys³ · Jens Christian Andersen³ · Søren Laurberg¹ · Lene H. Iversen¹

Received: 16 March 2017 / Accepted: 19 June 2017
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Abstract

Background Self-expanding metallic stent (SEMS) as a bridge to surgery for obstructive colorectal cancer may cause perforation of the tumor and thereby induce tumor spread and increase risk of recurrence, and eventually death. Evidence of the prognostic impact of SEMS-related perforation is, however, sparse. We conducted a long-term follow-up study to compare characteristics, overall survival, and recurrence rates between patients with and without SEMS-related bowel perforation.

Method This long-term follow-up study included obstructive colorectal cancer patients treated with SEMS as a bridge to surgery during a 10-year period at two primary and tertiary referral centers. The primary outcome was overall survival, and the secondary outcome was recurrence. We compared mortality and recurrence in patients with and without SEMS-related perforations by Cox proportion hazard regression, adjusting for age, comorbidity, and disease stage. The recurrence risk was examined for patients undergoing curative resection and computed treating death as a competing risk.

Results From January 2004 to December 2013, 123 patients were treated with SEMS as a bridge to surgery. Of these patients, 15 (12%) had SEMS-related perforations.

Median follow-up was 4.8 years (range 0.0–10.9 years). The overall 5-year survival was 58% for the entire cohort, but 37 and 61% for patients with and without perforations, respectively, corresponding to an adjusted hazard ratio of 1.6 (95% CI 0.8–3.3) in favor of patient without perforation. The overall 5-year recurrence rate was 34%, but 45 and 33% for patients with and without perforation, respectively, corresponding to an adjusted hazard ratio of 1.4 (95% CI 0.5–3.7) in disfavor of patients with perforation.

Conclusion SEMS-related perforations are common and may be associated with decreased survival and increased recurrence, although estimates in this study were imprecise.

Keywords Colonic neoplasms · Gastrointestinal endoscopy · Surgery

An estimated 14% of colorectal cancer patients present with obstructive disease [1]. These patients need immediate management, which traditionally has been emergency surgery known to be associated with higher morbidity and mortality as compared with elective surgery [2, 3]. For years, the postoperative 30-day mortality after emergency surgery for colonic cancer has been 15% or higher in Denmark, whereas the 30-day mortality after elective surgery has decreased and since 2013 been less than 2% [4].

An alternative method to emergency surgery for treatment of obstructive colorectal cancer is the insertion of a self-expanding metallic stent (SEMS), which is technically successful in 86–90% of patients, clinically successful in 78–88% of patients and associated with a 30-day mortality of approximately 2% [5, 6]. SEMS may serve as a bridge to subsequent elective surgery, thereby converting high-risk emergency surgery to a more

✉ Tue Højslev Avlund
Tue.avlund@gmail.com

¹ Department of Surgery, Section of Coloproctology, Aarhus University Hospital, Tage-Hansens Gade 2, 8000 Aarhus, Denmark

² Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

³ Department of Surgery A, Aalborg University Hospital, Aalborg, Denmark

favorable elective operation in patients with acute obstruction [7, 8]. However, SEMS may be complicated by perforation of the tumor in approximately 5% of patients, which may affect long-term prognosis by inducing tumor spread [5, 6]. Three randomized controlled trials comparing SEMSs and emergency surgery have been prematurely terminated; one due to an excess rate of anastomotic dehiscence in the emergency surgery arm (30 vs. 0%) [9] and two due to unacceptable high complication rates in the SEMSs arm [10, 11]. In the latter two trials, successful placement of SEMS was reported in only 47 and 70% of the SEMS attempts, with immediate perforation in 7 and 4% of the patients, respectively. Of particular concern, the perforation rates increased to 33 and 19%, respectively, after including silent perforations detected by pathology examination of the surgical specimens [10, 11]. These high perforation rates founded speculations on the long-term consequences of SEMS use. The speculations have been supported by evidence of high recurrence rates in rectum cancer patients with intra-operative tumor perforation [12], increased circulation of tumor markers after SEMS insertion [13], and high recurrence rates after SEMS as a bridge to surgery in obstructive colorectal cancer [14, 15].

On this background, we conducted a cohort study with long-term follow-up of obstructive colorectal cancer patients treated with SEMS as a bridge to surgery to compare characteristics, overall survival, and recurrence rates between patients with and without SEMS-related bowel perforation.

Materials and methods

Setting

We conducted this cohort study among colorectal cancer patients treated with SEMS at the Department of Surgery, Aarhus University Hospital, or the Department of Surgery A, Aalborg University Hospital, Denmark. The study was approved by the Danish Data Protection Agency (Ref No. 2014-41-2870). According to Danish law approval from the Scientific Ethical Board was not needed. Both surgical departments are primary and tertiary referral centers for colorectal diseases. The catchment area of each hospital is approximately 350,000–450,000 inhabitants. At both hospitals, all SEMS procedures were performed or supervised by colorectal surgeons. SEMS was the primary treatment option used for patients with malignant colonic obstruction, located anal to the right colonic flexure. Colonic obstructions were diagnosed by a combination of lack of passage of stool and flatus, abdominal pain, and/or colonic dilatation on computed tomography (CT) scans. Selection of

type of SEMS was according to the type of stent being in stock at each hospital, which changed over time depending on local financial contracts.

Subsequent to SEMS placement, patients underwent diagnostic work-up including contrast CT imaging for disease staging. All patients with potentially curable colorectal cancer according to a multi-disciplinary team decision were offered tumor resection in an elective setting. If a patient experienced SEMS placement failure or perforation before the multi-disciplinary team decision, they were included if the acute resection was performed with curative intention.

Surgery for colorectal cancer was performed or supervised by colorectal surgeons.

Patients

We included all patients treated with SEMS as a bridge to surgery during the periods January 2004 to December 2013 in Aarhus, and January 2004 to December 2011 in Aalborg.

In Aarhus, patients treated with SEMS in the period January 2004–February 2010 were identified by reviewing all endoscopic and surgical procedures, as done previously by Iversen et al. [16]. From March 2010 onwards, patients treated with SEMS have been prospectively registered in a local database. In Aalborg, patients treated with SEMS had all been prospectively registered for the period January 2004 to December 2011. For all patients, we reviewed medical records including follow-up data until July 2015. Patients were included in our study if a SEMS was placed or attempted placed with the intention to serve as bridge to subsequent surgery.

We categorized patients according to the presence or absence of SEMS-related perforations. Perforations were defined either as clinical or as silent; clinical perforations were those that were immediately visible or symptomatic with subsequent surgery confirming the perforation, and silent perforations were those identified only by the pathologist during macroscopic and microscopic examination of the surgical specimen. All perforations, irrespective of their location in the bowel, in the period from attempted SEMS placement until surgery was considered SEMS related as the intended treatment was SEMS as a bridge to surgery.

Outcomes

The primary outcome was overall survival. The secondary outcome was recurrence of colorectal cancer. Recurrence was only investigated for patients who had a curative surgical resection, including tumor-free resection margins, verified by histopathologic examination subsequent to SEMS placement, including curative treatment of any

synchronous metastases. Recurrences were defined as ‘local’ if located in vicinity of the anastomotic area, as ‘peritoneal carcinomatosis’ in case of peritoneal seeding, or otherwise as ‘distant recurrence.’

Characteristics and covariates

We included a number of covariates to describe our patients. Comorbidity was summarized using the Charlson’s Comorbidity index (CCI) [17] and patients were classified into 4 groups: CCI 0 (no comorbidity), CCI 1 (low comorbidity), CCI 2 (moderate comorbidity), and $CCI \geq 3$ (severe comorbidity). SEMS placement was defined as technically successful when placement was achieved, and as clinically successful when also relieving symptoms of obstruction and thereby allowing surgery in an elective setting. Resections were categorized by type and according to the surgical approach (open or laparoscopic). Postoperative complications were classified using the Clavien-Dindo (CD) classification [18]. Only complications with a CD score of 2 or above were registered. Disease stage was classified according to the Union for International Cancer Control (UICC) classification.

Statistics

Descriptive characteristics were listed for all patients and by the presence or absence of SEMS-related perforation. Continuous variables were described using medians and range and compared using the Mann–Whitney *U* test. Categorical variables were described in absolute numbers and percentage, and compared using the *Chi* square test. We calculated postoperative 30-day mortality from date of surgical resection and compared the mortality rates using the students *t* test. To investigate long-term survival (primary outcome), we used the Kaplan–Meier method. We analyzed data according to the intention-to-treat principle and followed patients from the date of SEMS placement or attempt (named ‘SEMS placement’ afterwards) until death, emigration, or end of follow-up (01.07.2015). We compared mortality among patients with and without perforation using Cox regression, adjusting for age, comorbidity, and tumor UICC stage. To evaluate recurrence (secondary outcome), we restricted our analysis to patients with curative resection as defined above. We followed patients from the date of colorectal resection until the date of recurrence, death, emigration, or end of follow-up (01.07.2015). The recurrence risk was calculated, treating death as a competing risk. We compared recurrence among patients with and without perforation using Cox regression, adjusting for age, comorbidity, and tumor UICC stage.

Results

Characteristics

We identified a total of 123 patients with colorectal cancer treated with SEMS as a bridge to surgery (Table 1). The indication for SEMS placement was primary colorectal cancer presenting with bowel obstruction in 119 patients, development of bowel obstruction during the course of neoadjuvant radiotherapy in three patients with primary rectal cancer, and bowel obstruction occurring during diagnostic work-up for treatment strategy of liver metastases in one patient with UICC stage IV disease (primary colonic cancer).

Eighteen patients (14%) underwent tumor resection in an emergency setting: 4 patients because of immediate bowel perforation following SEMS attempt, 5 patients because of technical SEMS placement failure, 3 patients because of clinically SEMS failure, and 6 patients because of clinical bowel perforation during diagnostic work-up after SEMS placement (Fig. 1).

Perforation, surgery, and pathology

In total, 15 patients (12%) developed a bowel perforation during the time span from SEMS attempt/insertion to surgery, of which five (33%) were silent. In two patients, the perforations were located at the caecum as a blow-out perforation. These were included as SEMS-related perforation as the perforation occurred during the intended treatment with SEMS as a bridge to surgery. At time of tumor resection, 20 (16%) patients had metastatic disease, of whom one had a SEMS-related perforation. Tumor localization and resection type is listed in Table 2.

Pathological examination of resected specimens revealed pT4 tumors in 10 (67%) patients with perforations and in 44 (41%) patients without perforation. Curative resection was achieved in 12 (80%) patients with perforation and in 95 (88%) patients without perforation.

Postoperative complications and mortality

No patients died in the time span from SEMS to surgery, median 20 days (0–225 days). Within 30 days after surgery (i.e., colorectal resection), 40 (33%) patients experienced complications (Table 3). One patient died from peritonitis after acute resection because of stent perforation at the tumor site, and one patient died from aspiration after emergency surgery.

Overall survival and recurrence

Median follow-up after SEMS placement was 4.8 years (range 0.0–10.9 years). Overall 5-year survival from date

Table 1 Characteristics of patients with colorectal cancer obstruction treated with self-expanding metal stents, as a bridge to surgery, at two referral hospitals, Denmark 2004–2013

Patient characteristics	Total <i>n</i> = 123	Patients with SEMS-related perforation <i>n</i> = 15	Patients without SEMS-related perforation <i>n</i> = 108	P-value
Age (years), median (range)	70 (32–94)	76 (51–84)	68 (32–94)	0.151
Sex				0.646
Male	67 (55%)	9 (60%)	58 (54%)	
Female	56 (45%)	6 (40%)	50 (46%)	
Charlson comorbidity index (CCI)				0.665
No comorbidity, CCI = 0	70 (57%)	11 (73%)	59 (55%)	
Low comorbidity, CCI = 1	33 (27%)	3 (20%)	30 (28%)	
Moderate comorbidity, CCI = 2	12 (10%)	1 (7%)	11 (10%)	
Severe comorbidity, CCI ≥ 3	8 (6%)	0 (0%)	8 (7%)	
Caecal diameter (cm) before SEMS, median (range)	9.5 (5–17)	10.0 (6–12)	9.0 (5–17)	0.718
Length of stent				0.505
Short ≤8 cm	69 (56%)	9 (60%)	60 (55%)	
Long ≥9 cm	49 (40%)	5 (33%)	44 (41%)	
Unknown	5 (4%)	1 (7%)	4 (4%)	
Technical success of SEMS placement	114 (93%)	11 (73%)	103 (95%)	0.002
Inpatient stay after SEMS placement (days), median (range)	3 (0–48)	10 (1–48)	3 (0–36)	<0.001

Number (%) if not otherwise indicated

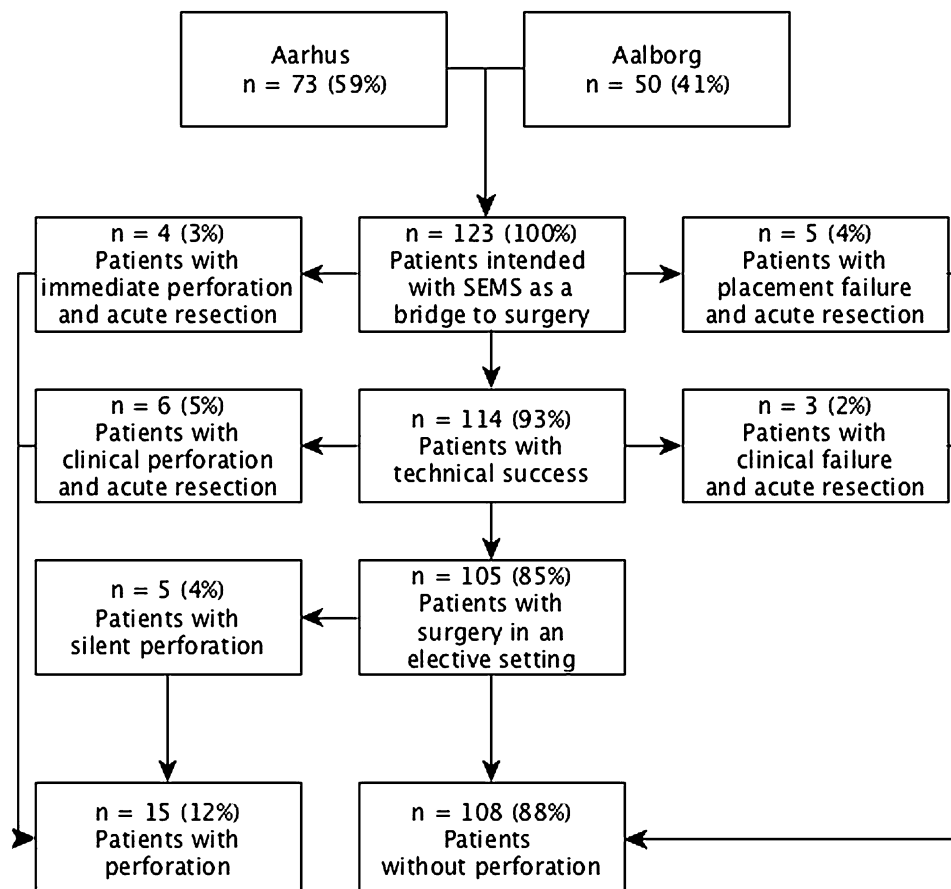
Fig. 1 Flow chart of patients with colorectal cancer obstruction intended treated with self-expanding metal stents as a bridge to surgery at two referral hospitals, Denmark 2004–2013

Table 2 Surgery and pathology in patients with colorectal cancer obstruction treated with self-expanding metal stents as a bridge to surgery, at two referral hospitals, Denmark 2004–2013

	Total <i>n</i> = 123	Patients with SEMS-related perforation <i>n</i> = 15	Patients without SEMS-related perforation <i>n</i> = 108	<i>p</i> -value
Elective resection	106 (86%)	5 (33%)	100 (93%)	<0.001
Tumor localisation				0.417
Hepatic flexure	2 (2%)	0 (0%)	2 (2%)	
Transverse colon	14 (11%)	1 (7%)	13 (12%)	
Splenic flexure	15 (12%)	1 (7%)	14 (13%)	
Descending colon	14 (12%)	4 (26%)	10 (9%)	
Sigmoid colon	63 (51%)	8 (53%)	55 (51%)	
Rectum	15 (12%)	1 (7%)	14 (13%)	
Resection type				0.035
Total colectomy	14 (11%)	4 (27%)	10 (9%)	
Right hemicolectomy	2 (2%)	0 (0%)	2 (2%)	
Extended right hemicolectomy	3 (2%)	1 (6%)	2 (2%)	
Transverse colectomy	8 (7%)	0 (0%)	8 (7%)	
Left hemicolectomy	35 (29%)	3 (20%)	32 (30%)	
Sigmoid colectomy	37 (30%)	3 (20%)	34 (31%)	
Hartmann's procedure	9 (7%)	4 (27%)	5 (5%)	
Partial mesorectal excision	8 (7%)	0 (0%)	8 (7%)	
Total mesorectal excision	4 (3%)	0 (0%)	4 (4%)	
Abdominoperineal excision	3 (2%)	0 (0%)	3 (3%)	
Surgical approach				0.123
Open	108 (88%)	15 (100%)	93 (86%)	
Laparoscopic	15 (12%)	0 (0%)	15 (14%)	
Stoma formation				0.062
Temporary	11 (9%)	3 (20%)	8 (7%)	
Permanent	31 (25%)	6 (40%)	25 (23%)	
Days from SEMS to operation, median (range)	20 (0–225)	3 (0–196)	22 (0–225)	0.001
Inpatient stay after operation (days), median (range)	8 (1–95)	9 (4–47)	7 (1–95)	0.048
pT-stage				0.162
T2	1 (1%)	0 (0%)	1 (1%)	
T3	68 (55%)	5 (33%)	63 (58%)	
T4	54 (44%)	10 (67%)	44 (41%)	
pN-stage				0.297
N0	67 (54%)	8 (53%)	59 (55%)	
N1	33 (27%)	6 (40%)	27 (25%)	
N2	23 (19%)	1 (7%)	22 (20%)	
Stage				0.699
UICC I	1 (1%)	0 (0%)	1 (1%)	
UICC II	62 (50%)	8 (53%)	54 (50%)	
UICC III	40 (33%)	6 (40%)	34 (31%)	
UICC IV	20 (16%)	1 (7%)	19 (18%)	
Curative resection	107 (87%)	12 (80%)	95 (88%)	0.390

Number (%) if not otherwise indicated

Table 3 Postoperative complications within 30 days after colonic resection in patients with colorectal cancer obstruction treated with self-expanding metal stents as a bridge to surgery, number (%) if not otherwise indicated

Complications	Total <i>n</i> = 123	Patients with SEMS-related perforation <i>n</i> = 15	Patients without SEMS-related perforation <i>n</i> = 108	<i>p</i> -value
No. of patients with complications	40 (33%)	6 (40%)	34 (32%)	0.509
Complications according to Clavien-Dindo grade				0.693
II	7 (6%)	1 (7%)	6 (6%)	
III	26 (21%)	3 (20%)	23 (21%)	
IV	6 (5%)	1 (7%)	4 (4%)	
V	2 (2%)	1 (7%)	1 (1%)	
Specific complications ^a				
Anastomotic leak	9 (7%)	1 (7%)	8 (7%)	0.978
Intra-abdominal abscess	11 (9%)	1 (7%)	10 (9%)	0.742
Wound abscess	13 (11%)	2 (13%)	11 (10%)	0.710
Peritonitis	2 (2%)	2 (13%)	0 (0%)	0.001
Kidney failure requiring dialysis	2 (2%)	2 (13%)	0 (0%)	0.001
Pneumonia	10 (8%)	2 (13%)	8 (7%)	0.431
Respiratory failure requiring artificial respiration >2 days	3 (2%)	1 (7%)	2 (2%)	0.257
Other ^b	19 (15%)	0 (0%)	19 (18%)	0.077

^a Same patient may be counted more than once

^b Included intestinal obstruction requiring surgery (*n* = 1), wound dehiscence (*n* = 4), afterbleeds requiring surgery (*n* = 3), stoma complication requiring surgery (*n* = 3), apoplexia cerebri (*n* = 1), urinary tract infection causing sepsis (*n* = 3), acute myocardial infarction (*n* = 1), aspiration (*n* = 1), deep vein thrombosis verified by ultra sound (*n* = 1), and pulmonary embolus (*n* = 1)

of SEMS placement for the entire cohort was 58% (95% CI 49–67%). In patients who had SEMS-related bowel perforation, the 5-year survival was 37% (95% CI 11–62%) compared to 61% (95% CI 51–71%) among patients without perforation. There was non-significantly higher risk of mortality among patients with SEMS-related bowel perforation as estimated by an adjusted hazard ratio of 1.6 (95% CI 0.8–3.3), *p* = 0.21.

Of the five patients who were acutely resected due to technical SEMS failure (without perforation) three died within 1.3 years of SEMS placement, whereas the two others survived for more than five years and had no recurrence during the follow-up period.

In total, 107 patients underwent curative resection and were followed up for recurrence. Their median follow-up was 4.3 years (range 0.0–10.9 years). The 5-year recurrence rate after curative resection was 33% (95% CI 24–42%) for the entire cohort. For patients with a SEMS-related perforation, the recurrence rate was 42% (95% CI 15–67%) as compared to 32% (95% CI 22–41%) among those without a SEMS-related perforation. The adjusted hazard ratio for recurrence was non-significantly higher in patients with perforation (1.4, 95% CI 0.5–3.7), *p* = 0.54. The types of recurrence are listed in Table 4; no patients were diagnosed only with local recurrence.

Discussion

In a cohort of obstructive colorectal cancer patients treated with SEMS as a bridge to surgery and with long-term follow-up, we observed an overall 5-year survival of 58% despite a SEMS-related bowel perforation rate of 12%. Characteristics of patients with and without SEMS-related perforation were almost comparable, although more patients who did not develop perforation suffered from severe comorbidity or presented with UICC stage IV disease. Patients with SEMS-related perforation had a lower 5-year survival of 37% compared to 61% in patients without perforation. In adjusted analysis, the decreased survival of patients with perforation was non-significant with a hazard ratio of 1.6 (95% CI 0.8–3.3). Similarly, after curative resection, patients who had SEMS-related bowel perforation had a higher 5-year recurrence rate of 45% compared to 33% in patients without perforation. The hazard ratio for recurrence was also non-significant: 1.4 (95% CI 0.5–3.7).

The impact of SEMS-related perforation on long-term survival of patients with obstructive colorectal cancer has to our knowledge not previously been the primary aim of an investigation. Existing evidence is based on studies comparing patients treated by acute surgical resections and

Table 4 Survival and recurrence in patients with colorectal cancer obstruction treated with self-expanding metal stents as a bridge to surgery at two referral hospitals, Denmark 2004–2013

	Total <i>n</i> = 123	Patients with SEMS-related perforation <i>n</i> = 15	Patients without SEMS-related perforation <i>n</i> = 108	<i>p</i> -value
SEMS as bridge to surgery (no.)				
30-day mortality (95% CI)	2% (0;6%)	7% (0;32%)	1% (0;5%)	0.097
Follow-up (years), median (range)	4.8 (0.01–10.9)	4.1 (0.03–10.3)	4.9 (0.01–10.9)	
Median survival (years) (95% CI)	6.0 (3.9;8.1)	4.3 (2.9;5.7)	6.5 (4.6;8.4)	
Survival				
3-year (95% CI)	79% (72;87%)	66% (42;90%)	81% (74;89%)	0.367
5-year (95% CI)	58% (49;67%)	37% (11;62%)	61% (51;71%)	0.367
Mortality rate ratio crude (95% CI)		1.4 (0.7;2.8)	1.00	0.370
Mortality rate ratio adjusted ^a (95% CI)		1.6 (0.8;3.3)	1.00	0.214
Patients with curative resection, who underwent follow-up for recurrence (no.)	<i>n</i> = 107	<i>n</i> = 12	<i>n</i> = 95	
Follow-up (years), median (range)	4.3 (0.01–10.9)	3.9 (0.03–10.3)	4.4 (0.01–10.9)	
Type of recurrence				0.640
Peritoneal carcinomatosis	8 (7%)	2 (17%)	6 (6%)	
Solid distant metastases	18 (17%)	2 (17%)	16 (17%)	
Peritoneal carcinomatosis and solid distant metastases combined	9 (8%)	1 (8%)	8 (8%)	
Recurrence				
3-year (95% CI)	25% (17;33%)	33% (10;59%)	24% (16;33%)	0.409
5-year (95% CI)	33% (24;42%)	42% (15;67%)	32% (22;41%)	0.409
Recurrence rate ratio crude (95% CI)		1.5 (0.6;3.9)	1.00	0.396
Recurrence rate ratio adjusted ^a (95% CI)		1.4 (0.5;3.7)	1.00	0.543

^a Rate ratio adjusted for age, comorbidity, and tumor UICC stage

patients managed with SEMS placement. In a meta-analysis of non-randomized studies, Matsuda et al. reported a 5-year overall survival of 57% after SEMS treatment and 67% after emergency surgery, with no statistical significant difference [19]. Our overall results for survival are largely comparable to the SEMS arm of these reports.

Three studies have reported both survival and recurrence with subgroup analysis for patients with colonic perforation related to SEMS [14, 20, 21]. In a study of patients younger than 75 years, Gorissen et al. reported overall survival rates of 71% after a median follow-up of 2.7 years among 62 patients treated with SEMS, and a recurrence rate of 32% after a median follow-up of 32 months among 38 patients [14]. Perforation was reported in 5 out of 62 patients (8%) treated with SEMS. Of these 5 patients, one died after surgery, 2 patients experienced recurrence, and 2 patients were disease-free at 3 years. Slothaak et al. reported long-term outcomes from the Dutch stent-in 2 trial, which was

terminated prematurely because of high rates of anastomotic leakage as well as a high number of perforations in the SEMS arm [20]. After 41 months, patients treated with SEMS as a bridge to surgery had an overall 4-year survival of 58%. Among the 6 patients with perforations, 4-year survival was 50% and 4-year recurrence rate was 83%. For patients without perforation (*n* = 20), 4-year survival was 62% and the 4-year rate of recurrence was 40%. Our results on survival and recurrence are largely comparable to these results. The third study reported increased risk of peritoneal seeding in patients with SEMS-related perforation during treatment. These results were based on three patients with perforation of whom one died shortly after resection, and should thus be interpreted with caution [21]. The high perforation rate in our study is likely explained by SEMS placement as the treatment of choice even in patients with complete colonic obstruction, and by the pathologists' attention on silent perforations. Perforations noted by the

pathologists alone account for approximately one-third in our study and half of the patients with perforation in the Dutch study [20].

It is still unclear whether patients with bowel obstruction caused by colorectal cancer should be treated with SEMs as a bridge to surgery or undergo emergency surgery. Although our study did not compare SEMs treatment with emergency surgery, our findings of low postoperative mortality are important in this context. Moreover, a Danish study among 2157 patients undergoing emergency surgery for colonic cancer between 2001 and 2005 found an overall 30-day mortality of 22.1% [1]. Another Danish study using nationwide data between 2005 and 2010 found a 30-day mortality of 13.7%, and a 5-year survival of 40.3% among 3333 patients undergoing emergency surgery for colorectal cancer [15]. This study also included 581 patients treated with SEMs and found no difference in 5-year survival, 49% (95% CI 42.6–54.6%), in patients with SEMs compared to patients undergoing emergency surgery 40% (95% CI: 38.1–42.6%). We present an overall 30-day mortality of 2% and a 5-year survival of 58% in a tertiary setting, which seems favorable compared to these results. These data should be seen in light of the persistently high 30-day mortality of at least 15% after emergency surgery for colorectal cancer in nationwide, population-based Danish studies [4].

The strengths of this study include long-term follow-up and the meticulous search strategy and registration to identify all patients attempted to have a SEMs placement. This methodology was used to ensure a high completeness of patients intended for treatment with SEMs, including patients where treatment was abandoned for technical reasons, a poor-prognosis subgroup likely not to be captured in register data.

Our study also had limitations. Even though the number of patients treated with SEMs in this study was relatively high compared with existing evidence, the number of events was low causing low precision of estimates. Furthermore, we adjusted for several potential confounding variables, but cannot rule out that our findings were still influenced by unmeasured confounding (e.g., smoking), or unknown confounding.

In conclusion, the bowel perforation rate after SEMs treatment as a bridge to surgery was high (12%). Although estimates were imprecise, SEMs perforation may have a negative impact in terms of survival and recurrence.

Compliance with ethical standards

Disclosure Tue Højslev Avlund, Rune Erichsen, Sissel Ravn, Zydrunas Ciplys, Jens Christian Andersen, Søren Laurberg, and Lene H. Iversen have no conflicts of interest or financial ties to disclose.

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