Digestive Endoscopy

Bridge-to-surgery versus emergency surgery in the management of left-sided acute malignant colorectal obstruction — Efficacy, safety and long-term outcomes

Eduardo Rodrigues-Pinto [a,*,1], Rui Morais [a,1], Catarina Coelho [b], Pedro Pereira [a],
Alessandro Repici [c], Guilherme Macedo [a]

[a] Gastroenterology Department, Centro Hospitalar São João, Porto, Portugal
[b] Gastroenterology Department, Faculty of Medicine, University of Porto, Porto, Portugal
[c] Gastroenterology, Humanitas Research Hospital & Humanitas University, Milan, Italy

ARTICLE INFO

ABSTRACT

Objective: Compare efficacy, safety and long-term outcomes of bridge-to-surgery and emergency surgery in acute malignant colorectal obstruction.

Methods: Retrospective study of 94 consecutive patients with left-sided acute malignant colorectal obstruction treated with curative intent between 2010–2017.

Results: 48 patients underwent stent placement and 46 underwent emergency surgery. Technical and clinical success were 100% and 87%. Laparoscopy and one-staged operation were more frequent in bridge-to-surgery (44% *vs* 2%, p < 0.001; 73% *vs* 30%, p < 0.001). Fewer permanent stomas were created in bridge-to-surgery (15% *vs* 35%, p = 0.013). Overall morbidity was 36%. Immediate and post-procedure stent related-complications occurred in 6% and 13%; surgery-related complications occurred in 28% (bridge-to-surgery: 15% *vs* emergency surgery: 41%, p = 0.004). No differences were found regarding tumor recurrence, recurrence-free survival and overall survival. R1 resection (HR 47.2, $_{95\%}$CI:4.1–543.7), number of lymph nodes harvested (HR 0.9 $_{95\%}$CI:0.8–0.99) and adjuvant therapy (HR 0.1 $_{95\%}$CI:0.01–0.9) predicted recurrence-free survival; pTMN stage IV (HR 7.3, $_{95\%}$CI:1.1–47.6), number of lymph nodes harvested (HR 0.90, $_{95\%}$CI:0.8–0.97), adjuvant therapy (HR 0.1, $_{95\%}$CI:0.02–0.4) and surgery-related complications (HR 5.3, $_{95\%}$CI:1.02–27.3) influenced overall survival.

Conclusion: Stent placement has a high success, similarly to emergency surgery, being associated with higher primary anastomosis and lower stoma rates. Tumor recurrence rate, recurrence-free survival and overall survival were comparable between groups; surgery-related complications influenced overall survival.

1. Introduction

Acute malignant colorectal obstruction (AMCRO) caused by advanced colonic cancer occurs in 8–29% of colorectal cancer patients [1], however, the management of this condition remains a major challenge in clinical practice [2]. Emergency surgery (ES) has been classically considered the conventional treatment, although associated with a mortality rate of 15–34% and morbidity of 32–64% [3]. Laparoscopic surgery is often considered infeasible in this setting, and a primary anastomosis is made in only 55% of patients [2]; ostomies are difficult to manage in these patients, taking into account that they are permanent most of the times [4,5].

Since its introduction in the early 1990s, self-expandable metal stents (SEMS) have been increasingly used as an alternative therapeutic option for AMCRO either palliatively or as a bridge-to-surgery (BTS) [6]. With BTS, ES can be converted into elective surgery, allowing improvement in the patient's clinical condition, adequate oncological staging, good colonic preparation, performance of an elective surgery by an experienced surgical team, the possibility of a laparoscopic approach and a smaller postponement in the initiation of chemotherapy [2,6]. This translates to preference of primary anastomosis over stoma construction or subtotal colectomy [7].

* Corresponding author at: Gastroenterology Department, Centro Hospitalar São João, Porto. Al. Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail address: edu.gil.pinto@gmail.com (E. Rodrigues-Pinto).
[1] The first and second author contributed equally in the design, conception, analysis, and paper writing.
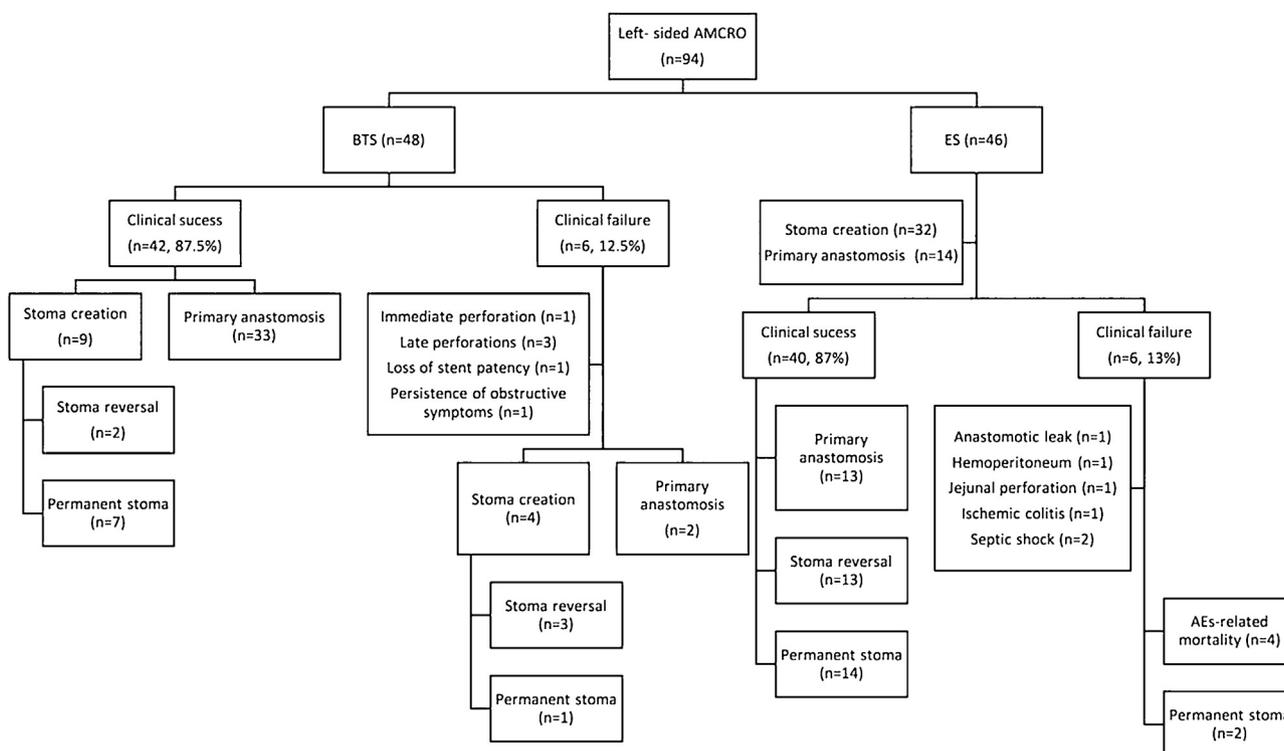
Fig. 1. Flowchart regarding management of patients with left-sided acute malignant colorectal obstruction.

On the other hand, colorectal stenting is difficult to perform and has a high rate of technical and clinical failure and adverse events (AEs) when performed by inexperienced hands. An overall AE rate up to 25% has been described [8–10], including pain, bleeding, perforation, inadequate expansion, migration, or re-obstruction (ingrowth/overgrowth). The most feared AE is perforation of the tumor with life-threatening abdominal sepsis and a possibility of oncological spillage, which eventually increases the risk of recurrence after curative surgery [11] and negatively affects the long-term survival [12]. In cases with SEMS-related colonic perforation, ES is required in most patients. In 2014, the European Society for Gastrointestinal Endoscopy stated against SEMS placement as a BTS [13]. Nevertheless, conflicting results were stated in three of the randomized controlled trials (RCTs) cited in the guideline [14]. Since then, several meta-analysis have been reported [15,16]; although SEMS placement as BTS seems to be effective and has some advantages over ES in the short-term, data regarding tumor recurrence rate raises concerns about the oncologic safety of stenting [15].

The contradicting data on the oncologic outcomes are the basis for the ongoing discussion on the long-term safety of colonic stents. With this study, we compared BTS and ES to evaluate the efficacy, safety and long-term outcomes of the two strategies in the management of AMCRO.

2. Material and methods

We performed a retrospective comparative cohort study of 94 consecutive patients with left-sided AMCRO, treated with a curative intent (as confirmed by the local multidisciplinary tumor board), in a tertiary center between January 2010 and December 2017. Patients' endoscopic and surgical management is illustrated in Fig. 1. The BTS group considers patients who underwent SEMS placement followed by elective surgery, whereas the ES group considers patients who underwent direct surgery. Preoperative, intra-operative, and post-operative care, including adjuvant ther-

apy protocols and follow-up, were carried out in accordance with the standard of care at our center and were the same for all patients. This study was approved by the Ethical Committee of our center.

Only patients with symptomatic AMCRO (absence of stool, abdominal pain, nausea and/or vomiting) whose final histological result was primary colon tumor, with the obstruction being located in the left-side colon (between splenic flexure and 5 cm from the anal verge) were included. Patients with resectable liver metastasis were also considered to have a curative perspective. Exclusion criteria were palliative intent, bowel perforation, inherited cancer syndromes and synchronous colon cancer.

Demographic characteristics (age, gender and ASA-score), medical history and ECOG were collected from medical records. In addition, surgical characteristics such as tumor location, TNM stage, number of lymph nodes harvested (LNH), type of resection and adjuvant therapy were collected. Other study outcomes included technical and clinical success rates, immediate and post-procedure AEs, primary anastomosis rate, colostomy rates, hospital stay, disease recurrence and overall survival. Surgery AEs were classified according to the Clavien-Dindo classification [17].

All the stents were uncovered (Hanarostent M.I.Tech Co., Inc, Seoul, South Korea) and were placed under direct visualization. The length of the stricture was measured fluoroscopically and the length of stent needed to cross the stricture was determined. The type of surgery and the extent of resection were determined by the surgeon, according to tumor location and stage and the general condition of the patient and included laparoscopic or laparotomic bowel resection, with or without creation of a stoma, according to surgeons' preferences and intra-operative findings.

SEMS technical success was defined as successful stent placement across the length of the stricture and the ability to pass stool. Clinical success was defined as resolution of obstructive symptoms after stent placement or ES without the need for additional interventions. ES in the BTS group was indicated in case of technical or clinical failure. Immediate AEs were defined as those occurring during stent placement or ES, while post-procedure AEs (local or

systemic) were defined as those occurring after technical success. Overall morbidity was defined as the occurrence of any immediate or post-procedure AE directly or indirectly related to SEMS placement (and subsequent resection surgery) or ES. Recurrence-free survival was defined as the time from the date of surgery to either cancer recurrence or the last follow-up without recurrence. Overall survival was defined as the time from the date of surgery to either death or the last follow-up visit.

2.1. Statistics

Categorical variables were described through absolute and relative frequencies and continuous variables were described as mean and standard deviation, median, percentiles, minimum and maximum. Hypotheses were tested about the distribution of continuous variables with non-normal distribution, by using the nonparametric Mann–Whitney and Kruskal–Wallis test, depending on the nature of the hypothesis. Cumulative survival was evaluated using survival analysis. The cumulative probabilities of survival were estimated using the Kaplan–Meier method by using LogRank test. Multivariable Cox proportional hazards regression models were used to test the independent association between clinical, procedure-related factors and survival after SEMS placement or ES.

All the reported p values were two-sided, and p values of <0.05 were considered statistically significant. All data were arranged, processed and analyzed with SPSS $^{\circledR}$ v.24.0 data (Statistical Package for Social Sciences).

3. Results

3.1. Baseline characteristics

From the 94 patients included in the study, 48 (51%) underwent SEMS placement and 46 (49%) underwent ES (Fig. 1). Baseline demographic, clinical and oncologic characteristics are summarized in Table 1. The majority of the tumors were located in the sigmoid colon (57%). A higher percentage of patients in the BTS group presented with stage IV disease (27% vs 4%, p = 0.004). The median follow-up was 25 months (IQR 11–51) (BTS: 24 months [IQR 8–37]; ES: 30 [IQR 14–60]).

3.2. Primary approach and surgical characteristics

Technical success was 100% with both approaches. Clinical success was 87%, with no significant differences between groups (BTS: 87% vs ES: 87%, p = 0.937). Reasons for clinical failure in the BTS group (n = 6; 12%) included perforation (n = 4), loss of stent patency (n = 1) and persistence of obstructive symptoms despite radiographic evidence of correct stent placement (n = 1), while in the ES group (n = 6; 13%) were septic shock (n = 2), anastomotic leak (n = 1), hemoperitoneum (n = 1), jejunal perforation (n = 1) and ischemic colitis (n = 1).

All patients in the BTS group underwent resection surgery, after a median time of 10 days (IQR 7–17), performed in the same hospitalization of SEMS procedure in 65%. There were significant differences in type of surgery performed (Table 1), with the preferred approach being sigmoidectomy in the BTS group (n = 14; 29%) and Hartmann procedure in the ES group (n = 24; 52%); laparoscopy and one-staged operation were performed more frequently in the BTS group (respectively, 44% vs 2%, p < 0.001 and 73% vs 30%, p < 0.001). Eighteen patients (5 in the BTS group and 13 in ES group) underwent stoma reversal with anastomosis creation, after a median time of 11 months (IQR 9–17). Significantly fewer permanent stomas were created in the BTS group (15% vs 35%, p = 0.013). The mean hospital stay after surgery was comparable between

Table 1
Baseline characteristics of patients with left-sided acute malignant colorectal obstruction undergoing self-expandable metal stent placement or emergency surgery and surgery performed in the bridge-to-surgery group and emergency surgery group.

	Total (n = 94)	BTS (n = 48)	ES (n = 46)	p Value
Gender				
Male	50 (53.2%)	25 (52.1%)	25 (54.3%)	0.826
Female	44 (46.8%)	23 (47.9%)	21 (45.7%)	
Age (median, years)	69 (58–80)	67 (58–76)	75 (60–83)	0.096
Age >75 years	34 (36.2%)	12 (25%)	22 (47.8%)	**0.021**
ECOG status				
0	61 (64.9%)	33 (68.8%)	28 (60.9%)	0.096
1	13 (13.8%)	9 (18.8%)	4 (8.7%)	
2	6 (6.4%)	3 (6.2%)	3 (6.5%)	
3	10 (10.6%)	3 (6.2%)	7 (15.2%)	
4	4 (4.3%)	0 (0%)	4 (8.7%)	
ASA score				
I	10 (10.6%)	7 (14.6%)	3 (6.5%)	0.708
II	40 (42.6%)	21 (43.8%)	19 (41.3%)	
III	23 (24.5%)	11 (22.9%)	12 (26.1%)	
IV	5 (5.3%)	2 (4.2%)	3 (6.5%)	
No data	16 (17.0%)	7 (14.6%)	9 (19.6%)	
Cardiovascular comorbidities	50 (53.2%)	24 (50.0%)	26 (56.5%)	0.526
Smoking habits	20 (21.3%)	14 (31.1%)	6 (14.6%)	0.071
pTNM stage				
I	2 (2.1%)	0 (0%)	2 (4.3%)	**0.013**
IIa	36 (38.3%)	11 (22.9%)	25 (54.3%)	
IIb	5 (5.3%)	3 (6.2%)	2 (4.3%)	
IIIa	1 (1.1%)	1 (2.1%)	0 (0%)	
IIIb	31 (33.0)%	18 (37.5%)	13 (28.3%)	
IIIc	4 (4.3%)	2 (4.2%)	2 (4.3%)	
IVa	11 (11.7%)	9 (18.8%)	2 (4.3%)	
IVb	4 (4.3%)	4 (8.3%)	0 (0%)	
Tumor location				0.326
Rectum	12 (12.8%)	7 (14.6%)	5 (10.9%)	
Sigmoid	54 (57.4%)	30 (62.5%)	24 (52.2%)	
Descending colon	28 (29.8%)	11 (22.9%)	17 (37.0%)	
Tumor length (median, cm)	4.4 (3.0–5.5)	4.5 (3.1–6.0)	4.2 (3.0–5.4)	0.773
Resection type				
Hartmann	30 (31.9%)	6 (12.5%)	24 (52.2%)	**<0.001**
Colostomy	3 (3.2%)	2 (4.2%)	1 (2.2%)	
Anterior resection	13 (13.8%)	11 (22.9%)	2 (4.3%)	
Sigmoidectomy	17 (18.1%)	14 (29.2%)	3 (6.5%)	
Left hemicolectomy	12 (12.8%)	11(22.9%)	1 (2.2%)	
Subtotal colectomy	13 (13.8%)	1 (2.1%)	12 (26.1%)	
Total colectomy	6 (6.4%)	3 (6.2%)	3 (6.5%)	
Surgical approach				
Laparotomy	68 (72.3%)	23 (47.9%)	45 (97.8%)	**<0.001**
Laparoscopy	22 (23.4%)	21 (43.8%)	1 (2.2%)	
Missing data	4 (4.3%)	4 (8.3%)	–	
Operation method				
Primary anastomosis	49 (52.1%)	35 (72.9%)	14 (30.4%)	**<0.001**
Stoma creation	45 (47.9%)	13 (27.1%)	32 (69.6%)	
Resection				
R0	81 (86.2%)	38 (79.2%)	43 (93.5%)	0.310
R1	9 (9.6%)	6 (12.5%)	3 (6.5%)	
Unknown	4 (4.3%)	4 (8.3%)	–	
Harvested lymph nodes (median)	18 (13–31)	22 (13–34)	16 (12–25)	0.212
Tumor differentiation				
Well	2(2.1%)	–	2 (4.3%)	0.222
Moderate	78 (83%)	39 (81.3%)	39 (84.8%)	
Poor	7 (7.4%)	2 (4.2%)	5 (10.9%)	
No data	7 (7.4%)	7 (14.5%)	–	

BTS: bridge-to-surgery; ES: emergency surgery; ECOG: Eastern Cooperative Oncology Group; ASA: American Society of Anaesthesiologists.
Bold values highlight the statistical significance between groups (p < 0.05).

Table 2
Clinical and oncological outcomes performed in the bridge-to-surgery group and emergency surgery group.

	Total (n = 94)	BTS (n = 48)	ES (n = 46)	p Value
SEMS AEs	–	9 (18.8%)	–	–
Surgery AEs	26 (27.7%)	7 (14.6%)	19 (41.3%)	**0.004**
Surgical AEs (Clavien-Dindo)				
0–II	14 (53.8%)	4 (57.1%)	10 (52.6%)	0.838
III–V	12 (46.2%)	3 (42.9%)	9 (47.4%)	
Surgery due to surgical AEs	10 (29.4%)	6 (42.9%)	4 (20%)	0.252
Overall morbidity	34 (36.2%)	14 (29.2%)	20 (43.5%)	0.149
Death related to SEMS and/or surgical AEs	5 (5.3%)	1 (2.1%)	4 (8.7%)	0.199
Post-procedure blood transfusion	12 (12.8%)	3 (6.3%)	9 (19.6%)	0.075
Blood transfusions (number of Units)	2 (1–2)	2 (1–2)	2 (1–2)	0.655
Hospital stay after surgery (median, days)	12 (7–19)	14 (7–18)	10 (7–20)	0.676
Total hospital stay, stent + surgery (median, days)	15 (9–20)	15 (13–20)	10 (7–20)	**0.003**
Permanent stoma	23 (25.8%)	7 (14.6%)	16 (34.8%)	**0.013**
Adjuvant therapy	51 (54.3%)	30 (62.5%)	21 (45.7%)	0.101
Tumor recurrence	29 (30.9%)	14 (29.8%)	15 (34.1%)	0.660
30-days mortality	5 (5.3%)	2 (4.2%)	3 (6.5%)	0.611
6-months mortality	13 (13.8%)	7 (13.8%)	6 (13.0%)	0.829
3-years mortality	34 (36.2%)	17 (35.4%)	17 (37.0%)	0.877

Bold values highlight the statistical significance between groups (p < 0.05).

Table 3
Self-expandable metal stents and surgery adverse events classified according to the Clavien-Dindo classification.

	BTS (n)	Clavien-Dindo	Management	ES (n)	Clavien-Dindo	Management
SEMS immediate AEs						
Migration	2	–	Second stent placement (2)	–	–	–
Perforation	1	–	Surgery	–	–	–
SEMS post-procedure						
AEs	2	–	Conservative (2)	–	–	–
Bleeding	3	–	Surgery (3)	–	–	–
Perforation	1	–	Surgery (1)	–	–	–
Stent obstruction						
Surgical AEs						
Local complications						
Rectovesical fistula	1	I	Conservative	–	–	–
Wound infection	2	II (2)	Antibiotherapy (2)	3	II (3)	Antibiotherapy (3)
Intra-abdominal abscess	3	II/IIIa/IVb	Percutaneous drainage (2), Antibiotherapy (1)	3	II (3)	Antibiotherapy (3)
Anastomotic dehiscence	–	–	–	1	V	Surgery
Colostomy dehiscence	1	V	Surgery	1	IIIb	Surgery
Hemoperitoneum	–	–	–	1	IIIb	Surgery
Peritonitis (jejunal perforation)	–	–	–	1	IIIb	Surgery
Ischemic colitis	–	–	–	1	V	Best supportive care
Ileus	–	–	–	2	I/II	Fluid therapy
Systemic complications						
Myocardial infarction	–	–	–	1	IVa	ICU admission
Respiratory insufficiency	–	–	–	1	IVa	ICU admission
Nosocomial pneumonia	–	–	–	1	II	Antibiotherapy
Nosocomial UTI	–	–	–	1	II	Antibiotherapy
Symptomatic tachycardia	–	–	–	1	II	Rhythm control therapy
Septic shock	–	–	–	2	V (2)	ICU admission (2)
Hypovolemic shock	–	–	–	2	IVa/IVb	ICU admission (2)

BTS: bridge-to-surgery; ES: emergency surgery; SEMS: self-expandable metal stents; AEs: adverse events; UTI: urinary tract infection; ICU: intensive care unit.

groups (BTS: 14 days vs ES: 10 days, p = 0.676). Nevertheless, the total hospital stay (SEMS plus subsequent resection surgery) was higher in the BTS group (15 days vs 10 days, p = 0.003).

3.3. Procedure-related morbidity

Overall morbidity was 36%, with no significant differences between groups (BTS: 29% vs ES: 43%, p = 0.149) (Table 2). Table 3 present a detailed overview of all AEs and their management. Thirteen percent of the patients had blood transfusions, with no significant differences between groups (BTS: 6% vs ES: 20%, p = 0.075).

In the BTS group, three patients (6%) had an immediate stent related-AE, including one perforation which occurred in a patient with stricture dilation prior to SEMS placement; 13% of the patients

(n = 6) experienced post-procedure AEs, after a median time of 4 days (2–10).

Surgery-related AEs occurred in 28% of all the patients (n = 26), being significantly lower in the BTS group (15% vs 41%, p = 0.004) (Table 2). In the BTS group, seven patients experienced surgery-related AEs – the patient with a colostomy dehiscence was admitted in the ICU after salvage surgery and died due to septic shock; two of the surgery-related AEs occurred in patients with previous SEMS AEs – one colovesical fistula in a patient with an immediate migration and one surgical wound infection in a patient with post-procedure perforation. In the ES group, 19 patients experienced surgery-related AEs – 13 local and 9 systemic – with four patients requiring salvage surgery; four of the patients died in relation to surgery-related AEs (one anastomotic dehiscence, one ischemic colitis and two septic shock).

Table 4
Clinical, procedure and oncologic predictors of disease recurrence after surgery and long-term survival after surgery.

	Disease recurrence after surgery				Long-term survival after surgery			
	Unadjusted HR (95% CI)	p Value	Covariate adjusted HR (95% CI)	p Value[*]	Unadjusted HR (95% CI)	p Value	Covariate adjusted HR (95% CI)	p Value[*]
Age								
<75 years	Ref.	0.418	–	–	Ref.	**0.004**	Ref.	0.159
≥75 years	1.36 (0.64–2.88)				2.51 (1.33–4.74)		4.57 (0.55–37.97)	
Gender								
Female	Ref.	0.608	–	–	Ref.	0.077	–	–
Male	1.22 (0.58–2.57)				1.79 (0.94–3.40)			
ASA								
<III	Ref.	0.706	–	–	Ref.	0.066	Ref.	0.293
≥III	1.18 (0.50–2.79)				1.94 (0.96–3.95)		1.89 (0.57–6.20)	
pTMN staging								
I–III	Ref.	0.139	Ref.	0.065	Ref.	0.377	Ref.	**0.037**
IV	2.13 (0.78–5.81)		5.04 (0.90–28.05)		1.45 (0.64–3.29)		7.33 (1.13–47.59)	
Tumor length	1.10 (0.91–1.35)	0.328	–	–	0.96 (0.79–1.17)	0.712	–	–
Resection								
R0	Ref.	0.003	Ref.	0.002	Ref.	0.203	Ref.	0.283
R1	5.33 (1.76–16.09)	**0.003**	47.19 (4.10–543.66)	**0.002**	1.98 (0.69–5.65)		3.10 (0.39–24.30)	
Harvested lymph nodes	0.95 (0.91–0.99)	**0.020**	0.90 (0.82–0.99)	**0.023**	0.97 (0.94–0.99)	**0.019**	0.90 (0.84–0.97)	**0.004**
Primary approach								
ES	Ref.	0.124	–	–	Ref.	0.656	–	–
SEMS	1.83 (0.85–3.96)				1.16 (0.61–2.18)			
SEMS-related AEs								
No	Ref.	0.681	Ref.	0.735	Ref.	0.470	Ref.	0.420
Yes	0.76 (0.20–2.83)		1.36 (0.23–8.15)		1.46 (0.52–4.08)		2.11 (0.34–13.07)	
Surgical AEs								
No	Ref.	0.856	Ref.	0.654	Ref.	0.071	Ref.	**0.047**
Yes	0.91 (0.35–2.41)		1.90 (0.11–31.86)		1.85 (0.95–3.61)		5.27 (1.02–27.29)	
Adjuvant therapy								
No	Ref.	0.895	Ref.	**0.036**	Ref.	**0.001**	Ref.	**0.002**
Yes	1.06 (0.48–2.34)		0.11 (0.01–0.87)		0.31 (0.16–0.60)		0.09 (0.02–0.42)	

ASA: American Society of Anaesthesiologists; ES: emergency surgery; SEMS: self-expandable metal stents; AEs: adverse events.
CI: confidence interval; HR: hazards ratio.
Bold values highlight the statistical significance between groups (p < 0.05).
  [*] p-Value: overall comparison between groups.

Table 5
Clinical, procedure and oncologic predictors of 30-days, 6-months and 3-years mortality.

	30-days mortality				6-months mortality				3-years mortality			
	Unadjusted OR (95% CI)	p Value	Covariate adjusted OR (95% CI)	p Value	Unadjusted OR (95% CI)	p Value	Covariate adjusted OR (95% CI)	p Value	Unadjusted OR (95% CI)	p Value	Covariate adjusted OR (95% CI)	p Value[*]
Age												
<75 years	Ref.	0.976	Ref.	0.485	Ref.	0.255	Ref.	0.508	Ref.	**0.015**	Ref.	0.423
≥75 years	1.0 (0.2–6.5)		0.4 (0.1–4.5)		1.9 (0.6–6.4)		2.6 (0.1–45.0)		3.0 (1.2–7.1)		2.29 (0.30–17.44)	
Gender												
Female	Ref.	0.246	–	–	Ref.	0.077	–	–	Ref.	**0.037**	Ref.	0.575
Male	3.7 (0.4–34.8)		–		3.4 (0.9–13.3)		–		2.6 (1.1–6.2)		1.60 (0.31–8.24)	
ASA												
<III	Ref.	0.133	–	–	Ref.	0.100	–	–	Ref.	0.104	Ref.	0.978
≥III	5.9 (0.6–59.6)		–		3.1 (0.8–12.3)		–		2.2 (0.8–5.9)		0.98 (0.2–5.3)	
pTMN staging												
I–III	Ref.	0.800	Ref.	0.669	Ref.	0.454	Ref.	0.230	Ref.	0.737	Ref.	0.181
IV	1.3 (0.1–12.9)		1.8 (0.1–29.2)		1.7 (0.4–7.2)		5.4 (0.3–84.0)		1.2 (0.4–3.8)		3.5 (0.6–22.3)	
Tumor length	0.7 (0.4–1.3)	0.286	–	–	0.9 (0.6–1.3)	0.576	–	–	1.1 (0.8–1.4)	0.605	–	–
Resection												
R0	Ref.	0.456	–	–	Ref.	0.416	–	–	Ref.	0.559	–	–
R1	2.4 (0.2–24.2)		–		2.0 (0.4–11.2)		–		1.5 (0.4–6.1)		–	
Harvested lymph nodes	0.9 (0.8–1.0)	0.091	0.9 (0.7–1.0)	0.065	0.9 (0.8–0.98)	**0.011**	0.8 (0.7–0.98)	**0.022**	0.97 (0.9–0.99)	**0.040**	0.9 (0.9–0.99)	**0.033**
SEMS AEs												
No	–	–	–	–	Ref.	0.094	Ref.	0.116	Ref.	0.171	Ref.	0.272
Yes	–		–		4.4 (0.8–24.7)		9.1 (0.6–141.6)		2.8 (0.6.12.4)		3.1 (0.4–22.4)	
Surgery AEs												
No	Ref.	**0.029**	Ref.	**0.023**	Ref.	**0.030**	Ref.	0.132	Ref.	0.216	Ref.	0.883
Yes	12.2 (1.3–114.8)		26.7 (1.6–457)		3.8 (1.1–12.7)		8.8 (0.5–148.2)		1.8 (0.7–4.5)		1.2 (0.2–8.0)	
Adjuvant therapy												
No	–	–	–	–	Ref.	**0.008**	Ref.	0.117	Ref.	**0.006**	Ref.	0.359
Yes	–		–		0.1 (0.03–0.6)		0.1 (0.01–1.7)		0.3 (0.1–0.7)		0.4 (0.1–2.6)	

ASA: American Society of Anaesthesiologists; SEMS: self-expandable metal stents; AEs: adverse events.
CI: confidence interval; OR: odds ratio.
Bold values highlight the statistical significance between groups (p < 0.05).
[*] p-Value: overall comparison between groups.

3.4. Long-term outcomes

Adjuvant therapy was performed in 54% (n = 51) of the patients, with no differences between groups (BTS: 62% *vs* ES: 46%, p = 0.101). Clinical and oncological outcomes are summarized in Table 2.

3.4.1. Disease recurrence

No differences were found regarding recurrence-free survival between BTS and ES groups (52 months *vs* 69 months, p = 0.119). In the multivariate Cox regression model, R1 resection (HR 47.2, $_{95\%}$CI 4.1–543.7), the number of LNH (HR 0.9 $_{95\%}$CI 0.8–0.99) and adjuvant therapy (HR 0.1 $_{95\%}$CI 0.01–0.9) were the only factors associated with recurrence-free survival (Table 4). SEMS and/or surgery-related AEs did not increase disease recurrence.

3.4.2. Survival

No differences were found between BTS and ES regarding overall survival (median: 37 months *vs* 55 months, p = 0.654) (Fig. 3), 30-days mortality, 6-months mortality and 3-years mortality (Table 2).

In the multivariate Cox regression model, pTMN stage IV (HR 7.3, $_{95\%}$CI 1.1–47.6), number of LNH (HR 0.90, $_{95\%}$CI 0.8–0.97), adjuvant therapy (HR 0.1, $_{95\%}$CI 0.02–0.4) and surgery-related AEs (HR 5.3, $_{95\%}$CI 1.02–27.3) were independently associated with survival estimate (Table 4).

In the multivariate logistic regression, 30-days mortality was only influenced by surgery-related AEs (OR 26.7, $_{95\%}$CI 1.6–456.97), while 6-months mortality and 3-years mortality were only influenced the number of LNH (respectively, OR 0.8, $_{95\%}$CI 0.7–0.98 and OR 0.92, 95% CI 0.86–0.99) (Table 5).

4. Discussion

The debate on the role of SEMS placement as a BTS for AMCRO remains open [2,15]; whether bridging with a SEMS should be the preferred treatment depends on the short and long-term outcomes. SEMS can convert an ES into an elective one, thus potentially reducing preoperative morbidity, restore bowel function, and avoid the need for a stoma, which is more often permanent rather than temporary and significantly diminishes the patient's quality of life [5]. However, several RCTs and case-matched studies have reported controversial results and expressed concern regarding the effect of stenting on short-term AEs and their effect on long-term survival in patients with potentially curable disease [5].

Stent placement is often difficult in patients with total obstruction or with tumors at an acute angle in relation to the lumen; for the benefits of colonic stenting to be observed, the skills and experience of the endoscopist in guidewire cannulation and stent deployment are of paramount importance. Our SEMS technical (100%) and clinical success (87%) rates were comparable or higher to previous similar studies (86–90% and 78–88%, respectively) [18], with no differences to the ES group arm. As expected, patients in the BTS group had more often a higher tumor stage. Even though preoperative stent placement did not affect overall morbidity rate (29% *vs* 43%), surgery-related AEs were significantly lower in the BTS group (15% *vs* 41%). Even though without significant differences, we would like to highlight that despite a higher need of surgery for AEs after SEMS plus surgery than after ES (43% *vs* 20%), death related to SEMS and/or surgical AEs was higher in the latter (2% *vs* 9%). This probably reflects a greater severity of the surgical AEs or a delay in diagnosis of surgery AEs; despite a reduction in mortality after ES during the past decades (15%–7%), elderly and frail patients still have a mortality risk up to 32% [2].

One of the firmly established advantages of SEMS as BTS is less temporary stoma formation. Furthermore, incisional hernias rates up to 30% following stoma closure have been reported in prospective studies, with approximately 50% of these patients eventually requiring surgical correction [19]. In our study, preoperative stent placement significantly improved laparoscopic operation (44% *vs* 2%), primary anastomosis rate (73% *vs* 30%), temporary stoma rate (27% *vs* 70%) and permanent stoma rate (15% *vs* 35%), comparable to Arezzo et al meta-analysis [15]. Considering the temporary stoma rate of 27% in our BTS cohort, it would be interesting to analyse which factors mattered in the choice for derivative colostomy as an elective procedure; perhaps the median time of 10 days between SEMS and elective surgery did not allow to effective decompress the colon; a retrospective analysis showed that stoma rate and anastomotic leakage rate may change according to the interval time between stent placement and surgery [20]. However, we should keep in mind that longer stents dwell times may result in an increased risk of microperforation and poorer oncological outcomes. Our stoma rate, however, is not different from other studies [21,22]. Besides, 38% of all BTS patients with a stoma, underwent later stoma revision with colonic reconstruction.

Regarding oncologic outcome, results remain controversial [10,23–27]. A retrospective study showed a 5-year overall survival rate significantly lower (25% *vs* 62%, p < 0.001), and a 5-year cancer-specific mortality rate significantly higher (48% *vs* 21%, p = 0.02) in the BTS group [27]. Another RCT found a 5-year overall recurrence rate higher in the BTS group (42% *vs* 25%, p = 0.027) [23]. In contrast to these results, Ceresoli et al. meta-analysis did not find differences in terms of local or systemic recurrence as well as 3- and 5-year survival [16], Arezzo et al. meta-analysis showed an increased risk of recurrence in the BTS group (40% *vs* 27%), although without statistical significance [15]. Possible reasons of different results in terms of oncologic outcome was showed in a follow-up analysis of the Dutch Stent-in 2 Trial in which disease-free survival and overall survival rate was worse in case of perforation [23]. Other factors besides perforation seem to affect the oncological outcome; a recent retrospective analysis showed that the occurrence of post-operative AEs after colorectal cancer resection, regardless of patient, disease and treatments factors, was associated with a shorter survival [28]. Our pooled tumor recurrence rate (30% *vs* 34%), recurrence-free survival (52 months *vs* 69 months) and overall survival (37 months *vs* 55 months) curves were comparable between the two groups. This might be related to the skills of the endoscopists and biliopancreatic background, as shown by an 87% clinical success rate with SEMS placement, which is higher than previous RCTs. Even though neither SEMS immediate AEs nor SEMS post-procedure AEs were associated with a higher rate of tumor recurrence, it is noteworthy that the 3 patients who experienced SEMS post-procedure perforation experienced tumor recurrence (1 at the anastomosis and 2 with distant metastasis). On the other hand, we must bear in mind that the oncological outcome in complicated ES may also be negatively affected by delayed or omitted adjuvant therapy, due to concerns surrounding wound healing and general well-being or the need for additional surgery [29]. In our series, although not significantly different, patients in the BTS group had a higher rate of adjuvant therapy as compared to those treated with ES (62% *vs* 46%); Ceresoli et al. meta-analysis reported similar outcomes (63% *vs* 54%) [16].

Perforation is the most feared complication — it may be caused by attempts to overcome the stenosis or it can occur after SEMS placement. Our BTS perforation rate was 8.3%. According to previous studies, the incidence of stent-related perforation ranges from 1.6% to 7.7% [30]. Reported consensus [31] recommend against balloon dilatation prior to SEMS placement because of its perforation risk. In our study, even though intraprocedural balloon dilatation was performed in only 2 patients, one of them experienced immediate perforation. Lee et al. suggested that patients should be observed for at least 3 days after stent placement for monitoring early adverse events [30]; however, our latest perforation occurred 9 days after SEMS placement.

To the best of our knowledge, only one previous study [11] analysed risk factors associated with disease recurrence and overall survival in patients with AMCRO. In our study, R1 resection, the number of LNH and adjuvant therapy estimated recurrence, while pTMN stage IV, surgery-related AEs, the number of LNH and adjuvant therapy estimated survival. Prognosis in CRC is clearly related to the degree of tumor infiltration through the bowel wall (pTNM), presence of lymph node involvement [32], as well as R1 resection and adjuvant therapy [33]. Many prospective studies have demonstrated a significant correlation between number of LNH, decreased recurrence and increased survival [34], being easy to accept that the greater the number of LNH, better is the prognosis; when more lymph nodes are examined, the chance of metastatic nodes detection increases, more patients receive adjuvant therapies, more patients receive detailed follow-up examination, and more patients undergo curative resection of recurrence [34]. We would like to highlight that only surgery-related AEs (and not SEMS AEs) influenced overall survival and 30-days mortality.

Limitations of our study include its retrospective nature, being conducted in a tertiary referral center (with an inherent risk of selection bias), and lack of data about quality of life. The decision to perform BTS or ES depended on surgeons and/or endoscopists preference. Despite previous studies on this topic, strengths of our study are the homogeneity between groups, the quite long follow-up period, as well as, the precisely description of outcome. Even though, although the majority of recurrences occur within 2 years of curative resection, our follow-up of 25 months may not capture disease progression at 5 years or late recurrences. In conclusion, SEMS placement was associated with a high technical and clinical success, similarly to ES, facilitating resection, as demonstrated by the higher primary anastomosis rate and lower stoma rates, with its possible positive effects on quality of life. Although not statistically significant, data regarding overall morbidity and death related to SEMS and/or surgical AEs showed a tendency to favor BTS compared with ES. Surgery-related AEs influenced overall survival and 30-days mortality; however, 75% of the patients with SEMS perforation experienced disease recurrence. As a result, to minimize the risk of inadvertent perforation, stenting should be performed only in units where experienced endoscopists are available. As SEMS placement may have an adverse impact on the oncologic outcomes in patients with a potentially curable tumor, until more long-term oncologic data become available, BTS cannot be established as the standard of care, and should be limited to centers where clinical and technical expertise is available. We should wait for 5-year outcomes of the Enteral Stents for Colonic Obstruction (ESCO) and Colo-Rectal Endoscopic Stenting Trial (CREST) trials, with special attention to the patients who experienced stent perforations.

Conflicts of interest

None of the authors acted as Reviewer or Editor of this article.

Dr. Alessandro Repici has consulting agreement with Boston Scientific. Dr. Eduardo Rodrigues-Pinto, Dr. Rui Morais MD, Dr. Catarina Coelho, Dr. Pedro Pereira and Prof. Guilherme Macedo have no conflicts of interest or financial ties to disclose.

References

[1] Imai M, Kamimura K, Takahashi Y, Sato T, Isokawa O, Maruyama M, et al. The factors influencing long-term outcomes of stenting for malignant colorectal obstruction in elderly group in community medicine. Int J Colorectal Dis 2018;33:189–97.

[2] van Halsema EE, van Hooft JE. Does short-term morbidity and stoma reduction outweigh a potential long-term risk of colonic stent placement? Gastrointest Endosc 2017;86:427–8.

[3] Fugazza A, Galtieri PA, Repici A. Using stents in the management of malignant bowel obstruction: the current situation and future progress. Expert Rev Gastroenterol Hepatol 2017;11:633–41.

[4] Nugent KP, Daniels P, Stewart B, Patankar R, Johnson CD. Quality of life in stoma patients. Dis Colon Rectum 1999;42(12):1569–74.

[5] Arezzo A, Balague C, Targarona E, Borghi F, Giraudo G, Ghezzo L, et al. Colonic stenting as a bridge to surgery versus emergency surgery for malignant colonic obstruction: results of a multicentre randomised controlled trial (ESCO trial). Surg Endosc 2017;31:3297–305.

[6] Cennamo V, Luigiano C, Coccolini F, Fabbri C, Bassi M, De Caro G, et al. Meta-analysis of randomized trials comparing endoscopic stenting and surgical decompression for colorectal cancer obstruction. Int J Colorectal Dis 2013;28:855–63.

[7] Cirocchi R, Farinella E, Trastulli S, et al. Safety and efficacy of endoscopic colonic stenting as a bridge to surgery in the management of intestinal obstruction due to left colon and rectal cancer: a systematic review and meta-analysis. Surg Oncol 2013;22:14–21.

[8] Sebastian S, Johnston S, Geoghegan T, Torreggiani W, Buckley M. Pooled analysis of the efficacy and safety of self-expanding metal stenting in malignant colorectal obstruction. Am J Gastroenterol 2004;99(10):2051–7.

[9] Ptok H, Meyer F, Marusch F, Steinert R, Gastinger I, Lippert H, et al. Palliative stent implantation in the treatment of malignant colorectal obstruction. Surg Endosc 2006;20:909–14.

[10] Small AJ, Coelho-Prabhu N, Baron TH. Endoscopic placement of self-expandable metal stents for malignant colonic obstruction: long-term outcomes and complication factors. Gastrointest Endosc 2010;71:560–72.

[11] Kim SJ, Kim HW, Park SB, Kang DH, Choi CW, Song BJ, et al. Colonic perforation either during or after stent insertion as a bridge to surgery for malignant colorectal obstruction increases the risk of peritoneal seeding. Surg Endosc 2015;29:3499–506.

[12] Kim HJ, Choi GS, Park JS, Park SY, Jun SH. Higher rate of perineural invasion in stent-laparoscopic approach in comparison to emergent open resection for obstructing left-sided colon cancer. Int J Colorectal Dis 2013;28:407–14.

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

[14] Kim MK. Is the ESGE guideline recommendation against the placement of stents for left-sided malignant colonic obstruction still open to debate? Endoscopy 2016;48:199.

[15] Arezzo A, Passera R, Lo Secco G, Verra M, Bonino MA, Targarona E, 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;86:416–26.

[16] Ceresoli M, Allievi N, Coccolini F, Montori G, Fugazzola P, Pisano M, et al. Long-term oncologic outcomes of stent as a bridge to surgery versus emergency surgery in malignant left side colonic obstructions: a meta-analysis. J Gastrointest Oncol 2017;8:867–76.

[17] 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;240:205–13.

[18] Avlund TH, Erichsen R, Ravn S, Ciplys Z, Andersen JC, Laurberg S, et al. The prognostic impact of bowel perforation following self-expanding metal stent as a bridge to surgery in colorectal cancer obstruction. Surg Endosc 2018;32:328–36.

[19] Amelung FJ, Ter Borg F, Consten EC, Siersema PD, Draaisma WA. Deviating colostomy construction versus stent placement as bridge to surgery for malignant left-sided colonic obstruction. Surg Endosc 2016;30:5345–54.

[20] Lee GJ, Kim HJ, Baek JH, Lee WS, Kwon KA. Comparison of short-term outcomes after elective surgery following endoscopic stent insertion and emergency surgery for obstructive colorectal cancer. Int J Surg 2013;11:442–6.

[21] Choi JH, Lee YJ, Kim ES, Choi JH, Cho KB, Park KS, et al. Covered self-expandable metal stents are more associated with complications in the management of malignant colorectal obstruction. Surg Endosc 2013;27:3220–7.

[22] Horesh N, Dux JY, Nadler M, Lang A, Zmora O, Shacham-Shmueli E, et al. Stenting in malignant colonic obstruction — is it a real therapeutic option? Int J Colorectal Dis 2016;31:131–5.

[23] Sloothaak DA, van den Berg MW, Dijkgraaf MG, Fockens P, Tanis PJ, van Hooft JE, et al. collaborative Dutch Stent-In study group. Oncological outcome of malignant colonic obstruction in the Dutch Stent-In 2 trial. Br J Surg 2014;101:1751–7.

[24] Kim HJ, Huh JW, Kang WS, Kim CH, Lim SW, Joo YE, et al. Oncologic safety of stent as bridge to surgery compared to emergency radical surgery for left-sided colorectal cancer obstruction. Surg Endosc 2013;27:3121–8.

[25] Choi JM, Lee C, Han YM, Lee M, Choi YH, Jang DK, et al. Long-term oncologic outcomes of endoscopic stenting as a bridge to surgery for malignant colonic obstruction: comparison with emergency surgery. Surg Endosc 2014;28:2649–55.

[26] Gorissen KJ, Tuynman JB, Fryer E, Wang L, Uberoi R, Jones OM, et al. Local recurrence after stenting for obstructing left-sided colonic cancer. Br J Surg 2013;100:1805–9.

[27] Sabbagh C, Browet F, Diouf M, Cosse C, Brehant O, Bartoli E, et al. Is stenting as "a bridge to surgery" an oncologically safe strategy for the management of

acute, left-sided, malignant, colonic obstruction? A comparative study with a propensity score analysis. Ann Surg 2013;258:107–15.

[28] Artinyan A, Orcutt ST, Anaya DA, Richardson P, Chen GJ, Berger DH. Infectious postoperative complications decrease long-term survival in patients undergoing curative surgery for colorectal cancer: a study of 12,075 patients. Ann Surg 2015;261:497–505.

[29] Verstockt B, Van Driessche A, De Man M, van der Spek P, Hendrickx K, Casneuf V, et al. Ten-year survival after endoscopic stent placement as a bridge to surgery in obstructing colon cancer. Gastrointest Endosc 2018;87, 705–713.e2.

[30] Lee YJ, Yoon JY, Park JJ, Park SJ, Kim JH, Youn YH, et al. Clinical outcomes and factors related to colonic perforations in patients receiving self-expandable metal stent insertion for malignant colorectal obstruction. Gastrointest Endosc 2018;87, 1548–1557.e1.

[31] Fernández-Esparrach G, Bordas JM, Giráldez MD, Ginès A, Pellisé M, Sendino O, et al. Severe complications limit long-term clinical success of self-expanding metal stents in patients with obstructive colorectal cancer. Am J Gastroenterol 2010;105:1087–93.

[32] Puppa G, Sonzogni A, Colombari R, Pelosi G. TNM staging system of colorectal carcinoma: a critical appraisal of challenging issues. Arch Pathol Lab Med 2010;134:837–52.

[33] Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, Aderka D, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol 2016;27:1386–422.

[34] Akagi Y, Adachi Y, Kinugasa T, Oka Y, Mizobe T, Shirouzu K. Lymph node evaluation and survival in colorectal cancer: review of population-based, prospective studies. Anticancer Res 2013;33:2839–47.