



Better recurrence-free survival after stent bridge to surgery compared to emergency surgery for obstructive left-sided colonic cancer in patients with stage III status of the American Joint Committee on Cancer (AJCC): a bicentric retrospective study

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Abstract

Purpose Stenting as a bridge to surgery (SBTS) can transform an emergency surgery (ES) into an elective surgery in patients with symptomatic left-sided malignant colonic obstruction. Concerns have been raised regarding short-term morbidity and long-term oncologic outcomes, with contrasting results reported in the literature. Our main aim is to evaluate not only long-term oncologic outcomes but also short-term postoperative outcomes of stented patients who underwent elective surgery compared to those who had ES.

Methods From January 2006 to May 2012, we retrospectively identified patients with confirmed left-sided colorectal cancer obstruction. This was done in two centers of reference of colorectal diseases in southern Spain with patients who were treated with curative intent either with ES or SBTS. The short- and long-term results were compared between both groups.

Results There were 71 patients in the stenting group and 66 in the emergency surgery group, with similar demographic data. Initial stoma creation rates were lower in the SBTS group (16.9% vs. 54.5%, $p < 0.005$) and the primary anastomosis rate was higher in the same group (83.1% vs. 45.5%, $p < 0.005$). Five-year recurrence-free survival (RFS) rates were comparable between groups (75.3 vs. 59.8%, $p = 0.220$), but RFS rates at 5 years for AJCC pathologic stage III were higher in the stenting group (69.7% vs 30%, $p = 0.004$). Both groups were comparable regarding overall and cancer-specific survival outcomes.

Conclusions The use of SBTS reduces ostomy rates in patients with obstructive colon malignancies. Long-term survival results are similar. Patients in the SBTS group with stage III AJCC status showed a higher 5-year recurrence-free survival rate than those in the ES group.

Keywords Colonic stenting · Bridge to surgery · Malignant left-sided colonic obstruction

Introduction

Colorectal cancer is one of the most common cancers worldwide, particularly in the economically developed world [1]. Colorectal obstruction as the first symptom at the time of diagnosis is reported in 10–30% of the patients, independently of the tumor stage [2–4].

This condition requires an emergency intervention, which has classically been emergency surgery (ES). Despite the medical and surgical advances, this emergency surgery still represents high morbidity (30–60%) and mortality (10–30%) compared with elective surgery (mortality rate less than 5%) [5–9].

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Self-expandable metal stents (SEMS) were initially used in palliation for patients with non-resectable malignant tumors due to their ability to achieve colonic decompression. Afterward, stents were accepted in patients with resectable colorectal obstructing tumors as a bridge to surgery with the aim of transforming an emergency surgery into an elective surgery. This allows stabilization of comorbidities and nutritional status and an accurate tumoral staging before surgery.

The outcome of the first two patients treated with this strategy was reported in 1994 by Tejero et al. [10]. Since then, this has been a recurring theme in scientific literature with many reviews which highlight its efficacy, especially in reducing ostomy rates [11–15], minimizing postoperative in-hospital stay, and reducing time to reintroduce oral diet and quality of life benefits [16].

However, this technique is not free of complications, such as perforation, migration, or obstruction [7, 17].

Moreover, concern still exists regarding oncological outcomes in patients whose disease is potentially curable due to the possible risk of both local progressions of cancer and metastatic spread. In particular, the direct effect of mechanical compression of the tumor could induce hematogenous spread and a higher risk of peritoneal involvement in the case of perforation [18–22].

At present, there are no consistent studies able to demonstrate that one strategy is superior to the other in terms of oncologic benefit with contrasting results reported in the literature. In this regard, the European Society of Gastrointestinal Endoscopy (ESGE) 2014 guideline does not consider the SEMS as a bridge to surgery as a standard treatment but it does consider it as an alternative to surgery in patients with an increased risk of postoperative mortality [23].

However, later publications to the 2014 ESGE guideline have demonstrated that long-term oncologic outcomes are comparable in patients treated with SEMS or ES for left-sided malignant colonic obstructions [16, 24].

The aim of our study is to compare short-term postoperative outcomes, long-term oncological outcomes, and survival in patients with potentially resectable left-sided malignant colonic obstruction who were treated with a stent bridge to surgery (SBTS) compared with those who were treated with emergency surgery (ES).

Methods

Patients and study design

We retrospectively reviewed patients with confirmed left-sided colorectal cancer, including upper rectum cancer diagnosed with clinically and radiologically confirmed obstruction, from two reference centers for colorectal disease in

southern Spain between January of 2006 and May of 2012. We identified 296 patients with left-sided malignant obstruction (LMO) at Virgen de la Victoria University Hospital (Málaga) and 335 at Virgen Macarena University Hospital (Sevilla). After applying exclusion criteria, 137 patients were included in the study: 71 patients in the SBTS group and 66 in the ES group. We then compared baseline characteristics, perioperative results, and oncological outcomes between the two hospitals, finding no statistically significant differences and achieving a homogeneous sample suitable for analysis.

For all patients, we assessed at least 5 years follow-up reviewing medical records from surgery or oncology departments. Patients were followed up according to established protocols and medical rounds included medical record, physical examination, carcinoembryonic antigen level, computerized tomography, magnetic resonance, or colonoscopy analysis when indicated.

Clinical symptoms of obstruction were defined as constipation, vomiting, or abdominal pain. Signs of obstruction were defined as proximal bowel or transitional zone distension, as well as a collapsed distal bowel on abdominal CT scan.

We excluded patients with colon perforation at the time of diagnosis, malignant obstruction in right or transverse colon, metastatic disease in spite of the location, or potential resectability of lesions. We also excluded mid to lower rectal cancer due to the fact that stenting at this level may be less tolerated by patients.

This study was approved by the local ethics committee of medical research.

Stenting technique

SEMS was performed in a combined endoscopic and fluoroscopic approach. It was performed by an experienced, qualified endoscopist who was available at the endoscopy room during working hours. The stent size, length, and diameter were selected according to the length measured at the site of the obstruction, and uncovered SEMS were used. Broadly speaking, patients underwent cleansing enemas for bowel preparation and were awake during insertion but were under deep sedation with propofol if required.

A guidewire was inserted across the point of stenosis and beyond the obstruction. A water-soluble contrast was injected via a catheter (through the guidewire) to confirm intraluminal placement of the wire and measure the length of stenosis. SEMS (WallFlex® Colonic Stent; Boston Scientific, Natick, MA, USA) was deployed over the guidewire and correct positioning was confirmed by fluoroscopy. Patients whose stent placement failed or who developed complications after stenting proceeded to emergency surgery. Clinical success

was defined as the resolution of obstructive symptoms within 72 h after the procedure along with stool passage.

Emergency surgery

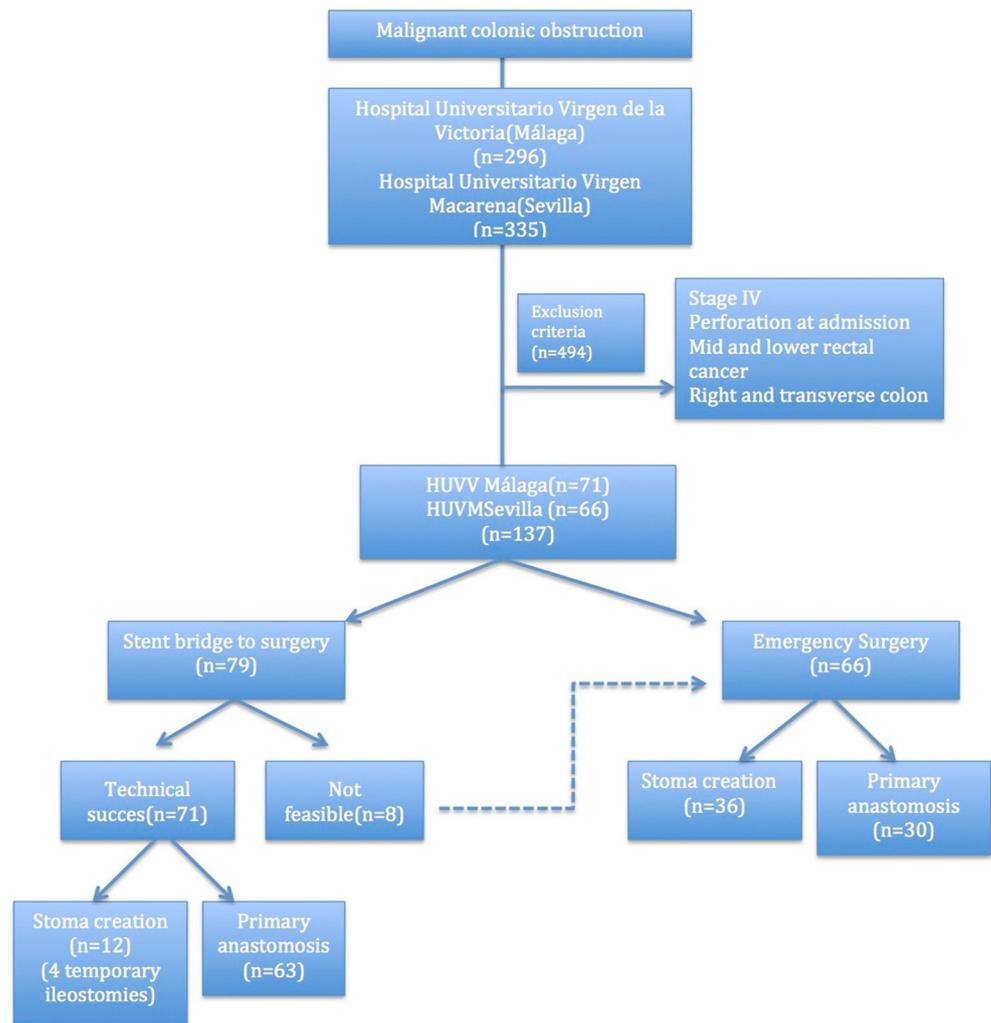
Patients who underwent emergency surgery were intervened at the earliest opportunity after initial stabilization by emergency surgeons. In both stented and emergency surgery procedures, tumor resection followed standard oncological principles. The type and extent of surgery were determined by the attending surgeon according to the location and stage of the tumor, as well as the patient’s general condition. The attending surgeon attempted single-stage resection with primary anastomosis. Hartmann’s procedure was performed if a primary anastomosis was not possible.

Once resolution of the obstruction was achieved, the medical condition of patients was optimized and thorough oncological workup was performed, including chest, abdomen, and pelvis CT scan, as well as pelvis magnetic resonance imaging (MRI) if indicated.

Statistical analysis

Numerical variables were expressed as the mean and standard deviation values and asymmetric distributions as medians and percentiles (P_{25} – P_{75}). Variables with no numerical values were expressed as percentages. Quantitative variable mean values were compared for groups using *t* test analysis for independent samples or the Mann-Whitney *U* test if variables showed non-normal distribution. Variable relation analysis was carried out by contingency tables using the χ^2 test or the Fisher test (exact). The interpretation of tables was made using the corrected typified residues. Kaplan-Meier curves and the Cox regression model were used for survival analysis. The Cox proportional-hazards model (HR) was used to analyze the correlation between potential risk factors and the three outcome models (recurrence-free survival, overall survival, and cancer-specific survival). Statistical significance was set at a *p* value of less than 0.05. Data were analyzed by an intention-to-treat approach, using the SPSS 24.0 software for Windows (SPSS Inc., Chicago, IL, USA).

Fig. 1 Flow chart with the study design and first post-intervention results



Results

SEMS insertion was attempted in 79 patients, but it was unsuccessful in eight cases due to complete obstruction and no possibility of introducing the guidewire through the stricture, representing a technical success rate of 89.8%. A flow chart is represented in Fig. 1. Clinical success was achieved in 60/71 patients (84.5%) due to 11 post-stenting perforations, 5 of which were silent and 6 ended in emergency surgery on the same day. There was no stent dislodgement or obstruction

reported. Patients with clinical failure due to complications were analyzed in the SEMS group on an intention-to-treat basis.

Baseline characteristics are shown in Table 1. There were no significant differences in age, gender, ASA score, tumor location, length, pathologic AJCC stages, or adjuvant chemotherapy/radiotherapy rates. We found a trend of higher median follow-up times for patients in the SBTS group ($p = 0.053$) and a poorer degree of tumor differentiation in the ES group ($p = 0.011$).

Table 1 Clinicopathologic characteristics of patients

	SBTS ($n = 71$) n (%)	ES ($n = 66$) n (%)	p
Sex			
Female	28 (39.4)	36 (54.5)	0.110
Male	43 (60.6)	30 (45.5)	
Median age	69 (61–77)	73.5 (62.5–81)	0.077
ASA score			
I	14 (19.7)	10 (15.2)	0.630
II	27 (38.0)	22 (33.3)	
III	28 (39.4)	30 (45.5)	
IV	2 (2.8)	4 (6.1)	
Median follow-up (months)	60 (0.06–240)	34 (0.03–123)	0.053
Tumor location			
Left colon	23 (32.4)	23 (34.8)	0.241
Sigmoid colon	32 (45.1)	36 (54.5)	
Rectosigmoid union	4 (5.6)	3 (4.5)	
Upper rectum	12 (16.9)	4 (6.1)	
Tumor median length (min; max)	5 (2–10)	4 (2–10)	0.005
pT stage			
T1-2	8 (11.3)	14 (21.2)	0.276
T3p	45 (63.4)	36 (54.5)	
T4p	18 (25.4)	16 (24.2)	
pN stage			
N0	40 (56.3)	36 (54.5)	0.660
N1	19 (26.8)	15 (22.7)	
N2	12 (16.9)	15 (22.7)	
Pathologic AJCC stage			
I	6 (8.5)	10 (15.2)	0.430
II	34 (47.9)	27 (40.9)	
III	31 (43.7)	29 (43.9)	
QT rate	37 (52.1)	32 (48.5)	0.800
RT rate	11 (15.5)	4 (6.1)	0.135
Pathologic differentiation			0.011
Well	38 (53.5)	32 (48.5)	
Moderately	31 (43.7)	22 (33.3)	
Poorly	2 (2.8)	12 (18.2)	
Median CEA	3.2 (2.12–6.16)	2.6 (1.2–6.75)	0.293
Resected nodes	14 (8–18)	10.5 (7–17)	0.157
Metastatic nodes	0 (0–2)	0 (0–3)	0.486

Table 2 Perioperative data

	SBTS (<i>n</i> = 71)	ES (<i>n</i> = 66)	<i>p</i>
Primary anastomosis	59 (83.1)	30 (45.5)	< 0.005
Stoma at discharge	12 (16.9)	36 (54.5)	< 0.005
Median time (days) from admission to emergency procedure (P_{25} – P_{75})	1 (0–4)	0 (0–4)	0.310
Median time (days) hospitalization (P_{25} – P_{75})	20 (11–27)	15 (10–24)	0.140
Postsurgical complication rate	11 (15.5)	19 (28.8)	0.060
Postoperative complication type	7 (63.6)	10 (52.6)	0.688
Postoperative sepsis	3 (27.3)	5 (26.3)	
Anastomosis leak	1 (9.1)	4 (21.1)	
Paralytic ileus			
Reintervention rate	2 (2.8)	9 (13.8%)	0.018
In-hospital 30-day mortality	5 (7.0)	5 (7.6)	0.905

Initial stoma creation rates, including temporary ostomies, were lower in the SBTS group (16.9% vs. 54.5%, p value < 0.005). Five out of 36 patients with a stoma at the time of discharge in the ES group underwent planned surgery to restore the intestinal transit and close the stoma.

In addition, a higher primary anastomosis rate was found in the SBTS group compared to the ES group (83.1% vs. 45.5%, p < 0.005) with a stent insertion to a programmed surgery median time of 13 days (1–184) (Table 2).

There was no difference between both groups regarding median time from admission to the emergency procedure, 1 day for the stenting group and 0 days for the surgery group (p = 0.310). The median time of hospitalization was also comparable (20 vs. 15 days, p = 0.140).

There was a significantly lower reintervention rate due to complications in the stenting group compared to the surgery group (2.8% vs. 13.8%, p = 0.018).

In terms of postoperative complications, there was a clear trend towards statistical significance (p = 0.060) favoring the stenting group, with 11 (15.5%) complications and 29

(28.8%) in the ES group. The most common complication for both groups was postoperative sepsis, followed by anastomosis leakage and paralytic ileum, without statistically significant difference between both groups (p = 0.688). Thirty-day mortality rates during hospital stay were similar between groups (7.0% vs. 7.6%, p = 0.140).

Table 3 shows the recurrence and mortality outcomes. We found no difference between groups in recurrence rates (34.8% vs 19.7%, p = 0.072) and recurrence location when discerning between local and distant recurrence (p = 0.999). There was a trend towards a longer recurrence-free follow-up time (58 vs. 24 months, p = 0.053) in the SEMS group. However, 5-year recurrence-free survival (RFS) rates were comparable between groups (75.3% vs. 59.8%, p = 0.220) (Fig. 2).

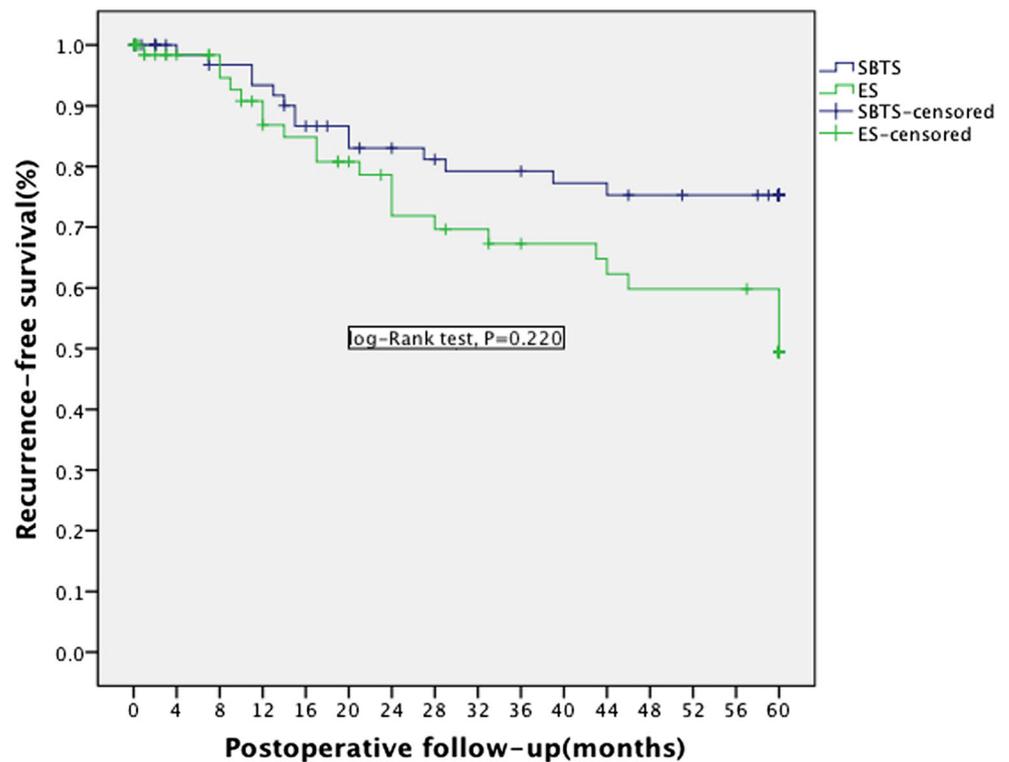
We performed a subgroup analysis according to the AJCC pathologic stage and found a higher 5-year RFS rate for stage III patients in the stenting group (69.7% vs. 30%, p = 0.004) (Fig. 3). No differences were found for AJCC stages I and II.

Multivariate analysis correcting for known risk recurrence factors is shown in Table 4.

Table 3 Oncologic recurrence and mortality outcomes

	SBTS (<i>n</i> = 71)	ES (<i>n</i> = 66)	<i>p</i>
Global recurrence rate	14 (19.7)	23 (34.8)	0.072
Recurrence location			0.999
Local	8 (57.1)	13 (56.5)	
Distant	6 (42.8)	10 (43.5)	
Liver	4 (28.6)	4 (17.4)	
Lung	0 (0)	6 (26.1)	
Peritoneal	3 (21.4)	6 (26.1)	
Other	2 (14.3)	0 (0)	
Colon	5 (35.7)	7 (30.4)	
Median follow-up (months) free of recurrence	58 (0.06–240)	24 (0.03–123)	0.053
Global mortality rate	29 (40.8)	37 (56.1)	0.075
Non-cancer-related mortality rate	11 (15.5)	14 (21.2)	0.386
Cancer-specific mortality rate	19 (26.8)	23 (34.8)	0.401

Fig. 2 Kaplan-Meier curve of RFS for the SBTS and ES groups. The 5-year RFS rates were comparable between groups (log-rank test, $p = 0.220$)



There were no statistical differences in overall mortality, non-related cancer mortality, and cancer-specific mortality ($p = 0.075$, $p = 0.386$, and $p = 0.401$, respectively), as shown

previously in Table 3. There was a trend towards statistical significance for longer follow-up times for the SBTS group, 60 vs. 34 months ($p = 0.053$).

Fig. 3 Kaplan-Meier curve of RFS for the SBTS and ES groups according to the pathologic AJCC Stage III. The 5-years RFS rate was significantly higher in the SBTS group (log-rank test, $p = 0.004$)

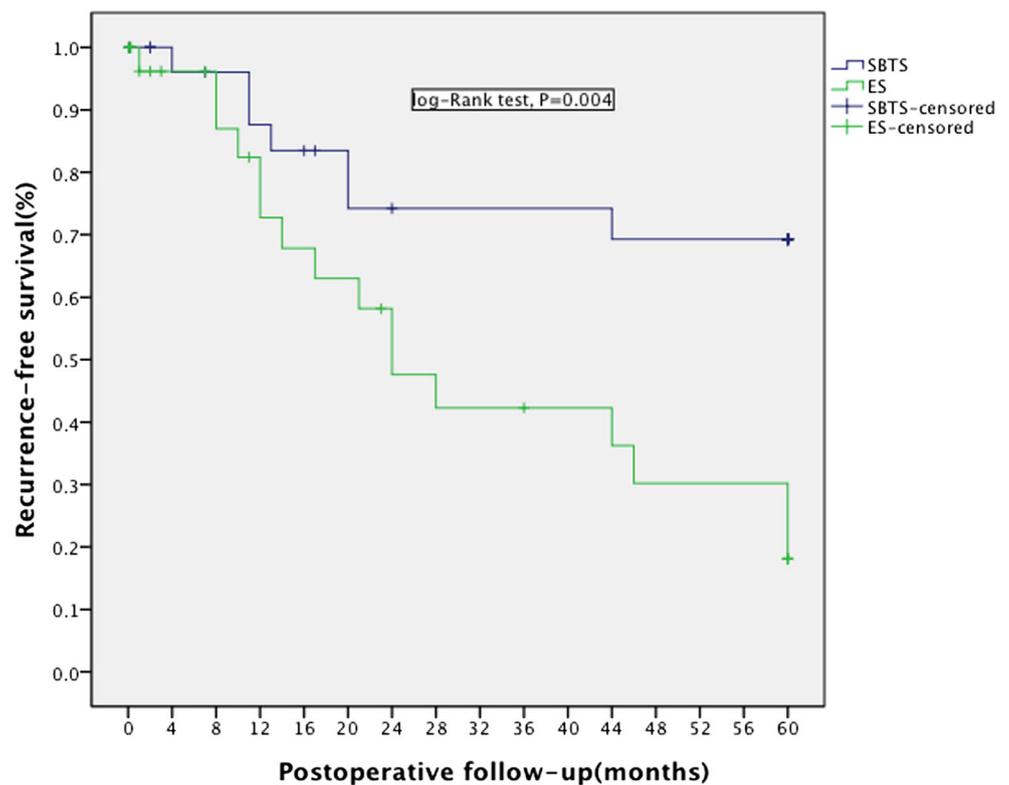


Table 4 Multivariate analysis of risk factors of recurrence

	HR	95% CI	<i>p</i>
SBTS	1		
ES	2.26	1.16–4.40	0.017
AJCC stage I or II	1		
AJCC stage III	2.18	1.07–4.44	0.032
Chemotherapy no	1		
Chemotherapy yes	2.79	1.16–6.71	0.022

Five-year overall survival (OS) was comparable between groups (42.6 vs. 57.7%, $p = 0.071$) as shown in Fig. 4. When performing subgroup analysis by AJCC stage status (stage I, $p = 0.150$; stage II, $p = 0.730$; stage III, $p = 0.840$), the 5-year OS was also comparable between groups.

Discussion

Patients with left-sided malignant colonic obstruction with AJCC stage III who undergo a SBTS show superior 5-year recurrence-free survival outcomes than those operated with emergency surgery, while long-term survival results are similar in both groups. The use of SEMS as a bridge to surgery reduces ostomy rates in patients with obstructive colon

malignancies and allows a higher rate of primary anastomosis, compared to those who have emergency surgery.

Our study has several limitations as its retrospective design with no randomization makes it difficult to standardize patient selection and the management protocol during the study. Elective surgeries were performed by colorectal surgeons, whereas emergency surgeries were performed by general surgery specialists.

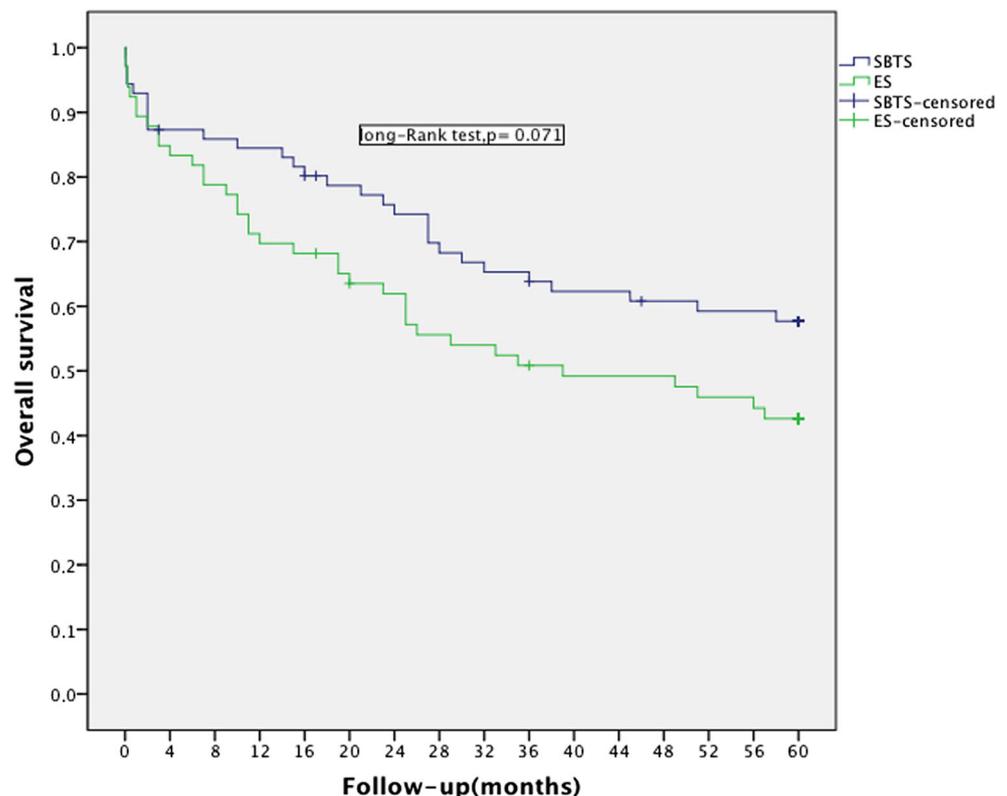
The strength of this study includes its sample size, similar to or higher than in other retrospective studies on the same issue. We also must recall that this is a bicentric study, with the previous comparison between centers and no differences between them regarding demographic and oncologic results, accurately representing the daily clinical practice.

Although SEMS insertion is widely used to relieve colorectal cancer obstruction, concerns still exist regarding oncological outcomes due to possible dissemination of the tumor through the stent [18].

In consideration of these concerns and controversial results in the literature, clinical practice guidelines do not recommend the use of SEMS as the standard treatment of symptomatic left-sided malignant colonic obstruction for patients with potentially curable but obstructing left-sided colonic cancer.

Stent placement is often difficult and depends on multiple factors, such as local expertise and clinical status including the level of obstruction. Some randomized trials have begun its

Fig. 4 Kaplan-Meier curve of OS for the SBTS and ES groups. The OS was comparable between groups (log-rank test, $p = 0.071$)



course, but they have been prematurely interrupted due to the unexpectedly high stent-associated risk of perforations [25, 26].

Thus, a recent meta-analysis showed lower technical and stenting clinical success rates than expected (70.7% and 69.0%, respectively) [13].

Our technical and clinical success rates were 89.8% and 84.5%, respectively, which are comparable to the results of other meta-analyses [17].

We observed 11 post-stenting perforations in our study (15.5%), which are higher when compared with the reported perforation rate of 4% [25, 27–29], but it did not affect negatively the postoperative and oncologic results. In fact, there was a trend to a higher postsurgery complications rate ($p = 0.060$) and a higher reintervention rate ($p = 0.018$) in the surgery group.

Regarding short-term overall morbidity and temporary and permanent stoma rates, a recent study [30] and several recent meta-analyses of randomized, controlled trials [15, 31] showed that SBTS brings about superior results compared to ES, offering significant advantages for primary anastomosis.

These results are comparable with the results in our study where the anastomosis rate was 83.1% in the SBTS group and 45.5% in the ES group ($p < 0.005$), and postoperative complications rate were lower in the stenting group, in contrast to the findings in previous studies [25, 32, 33].

The median time from stent insertion to programmed surgery in our study is 13 days, with a wide range (1–184) due to 15 tumors in the upper rectum that were treated with neoadjuvant radiotherapy and chemotherapy. This time interval is shorter than those reported in other studies [13].

Global mortality and 30-day mortality rates were comparable between our study groups, similar to those reported in other studies in the literature [34]. There was no difference in hospital stay lengths between groups either, meaning that the use of SEMS as a bridge to surgery does not prolong the course of patient management.

In our study, we found a trend towards longer disease-free follow-up time in the SBTS group but no differences in terms of recurrence and recurrence-free survival rates. The study performed by Kim et al. [21] reported a similar overall recurrence rate in both groups of patients (SBTS, 35%; ES, 35%; $p = 1$), with superior, yet nonsignificant results concerning 5-year disease-free survival (66.7% vs. 54.8%; $p = 0.948$) and 5-year overall survival (100% vs. 77.9%; $p = 0.103$) in the stenting group. Gorissen et al. [35] reported a higher rate of local recurrence in patients treated with SBTS, especially in younger subjects (32% vs. 8%).

The 5-year overall survival rate in our study was higher in the SBTS group (57.7 vs. 42.6, $p = 0.071$). Although it failed to show statistical significance, we could at least say that stent placement does not adversely affect long-term survival rates, as shown in a recent meta-analysis by Zhang et al. including

eight clinical trials [31]. Overall and cancer-specific mortality rates are also comparable between groups in our study, as shown in previous trials [21].

Concerns still exist regarding tumor dissemination related to colon perforation: In the stentin 2 trial, there was a non-significant benefit in the emergency surgery group concerning 4-year disease-free survival (SBTS 30% vs. ES 49%; $p = 0.149$) and 4-year overall survival (SBTS 58% vs. ES 67%; $p = 0.468$) regarding colon perforation after stenting [36]. However, these results have not been found in other studies with lower stent-related perforation rates. In our study, there were superior OS and RFS rates in the stenting group in spite of 11 stent-related perforations.

We observed a higher RFS for AJCC pathologic stage III in the SBTS group, where 5-year RFS was 69.7% vs. 30% ($p = 0.004$). As the AJCC stage III is characterized by the presence of metastatic nodes, a hypothesis to explain this result would be that difficult surgery in an emergency setting yields a poorer rate of lymph node resection compared to elective surgery. Other studies performing the same subanalyses with AJCC stages have failed to show significant differences [37].

Multivariate analysis correcting for known risk factors for recurrence such as AJCC staging and use of chemotherapy showed a recurrence hazard ratio of 2.26 [95% CI: (1, 16–4, 40); $p = 0.017$] for those who underwent ES compared to those in the SBTS group in contrast to the results in the trial by Gorissen et al. [31] where no factors were found to be significant for tumor recurrence in multivariate analysis.

Pulling together the results of this study, this approach seems to be a useful alternative to emergency surgery but future prospective studies will be helpful in defining the role of colonic stenting as a bridge to surgery. So although the internal validity of the study might be questioned, its external validity is clear and argues in favor of its application in emergency situations.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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