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ORIGINAL ARTICLE

Stent or surgery for incurable obstructive colorectal cancer: an individualized decisión

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Abstract
Introduction In the setting of stage-IV obstructive colorectal cancer, self-expanding metallic stents (SEMS) placement and palliative surgery may be appropriate options. The aim of the present study is to evaluate the long-term results of surgery compared with stent implantation and to identify patients in whom one of these options can provide more benefit.
Materials and methods From November 2000 to November 2008, 98 patients with incurable stage-IV colorectal cancer were treated with palliative surgery (n=53) or SEMS (n=45). Data were recorded with respect to age, gender, tumor location, carcinoembryogenic antigen, ASAclass, presence of metastatic disease in one or multiple organs, volume of liver metastases, urgency of the procedure and treatment with chemotherapy. Comparison between surgery and stent placement was performed for all group and for patients who received and did not receive chemotherapy.
Results Both groups were comparable regarding age, ASA-class, chemotherapy treatment, tumor location and presence of metastatic disease in one or multiple organs but not in gender, rate of urgent procedures, abnormal CEA and of volume of liver metastases >25%. Survival in surgical group was significantly higher (11.9 vs 7.3 months; log-rank test, p = 0.002). SEMS group had lower early morbidity, hospital stay and stoma creation. For patients who received chemotherapy, surgery provided benefit in survival (6.8 vs 3.9 months; log-rank test, p = 0.101); in this subgroup, long-term complications from the primary tumour were more common in stented group, and time to chemotherapy was longer in the group of surgery. No differences in survival were shown in patients who did not receive chemotherapy.
Conclusion Stent placement offers advantages regarding early morbidity, hospital stay and stoma creation. Surgery offers a benefit in survival in patients who receive chemotherapy but not in non-candidates to chemotherapy.

Keywords Incurable coloretal cancer · Self-expanding metal stent · Palliative surgery

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Introduction

About 20% of colorectal cancers are diagnosed as a disseminated disease, and the majority of metastatic patients have unresectable cancer. Classically, resection of the primary tumour and postoperative chemotherapy was the standard of treatment. Although chemotherapy (ChT) seems to be an appropriate option for patients without symptoms of the primary tumour, the best strategy for patients with colonic obstruction and incurable metastases remains unclear.

Since the purpose of surgery in this setting is palliative, the use of self-expanding metallic stents (SEMS) would seem reasonable. A review shows that insertion of self-

expanding stents can be done with low morbidity and mortality [1]. To avoid stoma creation and a faster recovery are the main reasons in favour of this technique.

On the other hand, patients might need surgery or endoscopic procedures due to complications of unresected primary tumours. Resection of colorectal primary cancer is intended to avoid posterior complications and to allow uninterrupted ChT treatment, but high mortality rates, ranging between 7% and 22% [2] have been reported. By-pass or stoma creations are other alternatives, but for patients with poor prognosis, SEMS might be the best option.

The aim of this study is to compare long-term results of patients with colonic obstruction and incurable metastases treated with SEMS placement or surgery.

Materials and methods

Since November 2000 to November 2008, 163 patients with incurable stage IV colorectal cancer were evaluated. In this study, we include 98 consecutive patients who had obstructive symptoms and were treated either with surgery (group A) or SEMS placement (group B). Patients with non-colorectal synchronous tumours were excluded.

The diagnosis of large bowel obstruction was made clinically and radio-logically. Distant staging included computed tomography of the abdomen and pelvis and a chest x-ray. The decision whether to do surgery or to place a stent and about the type of surgery was made by the admitting surgeon or by the Digestive Oncology Committee of Hospital de Navarra. Assessment of non-resectable liver or lung metastases was made by the surgeon in charge of the patient and the Digestive Oncology Committee of our hospital. Tumour location was classified as right colon cancer (if tumour was proximal to splenic flexure), left colon cancer (if tumour was distal to splenic flexure) and rectal cancer (if tumour was in the lowest 15 cm of the large bowel). If the surgical or endoscopic procedure was performed within the first 72 h after hospital admission, the procedure was considered urgent. Liver metastases were found in 91 patients, being isolated liver metastases in 64 cases; in seven patients, metastases were found in the peritoneum.The survival of patients was calculated from the time of diagnosis.

Surgery was performed in 53 patients. The surgical technique was decided by the surgeon depending on the extent of disease and general condition of the patient.

SEMS placement was performed in 45 patients. Stenting was always performed with the patient sedated (propofol e.v.) and under endoscopic and fluoroscopic control. Once the tumoral stricture was endoscopically identified, a stiff guide wire (SS Jagwire, Boston Scientific, USA) was advanced across the stricture. In some cases of tumours located at the level of a flexure and, therefore, difficult to face with the endoscope, the guide wire was advanced with the aid of a sphincterotome. Right colon cancer was not a contraindication for stent placement but SEMS were not inserted in low third (5 cm) rectal cancer. Dilation was never indicated in order to minimize the potential risk of colonic perforation. A nitinol uncovered stent (Hanarostent, M.I. Tech, Korea) was inserted through the working channel of the endoscope, advanced over the guide wire and finally released with the aid of fluoroscopy. Stent length was adjusted to the stricture characteristics. After stenting, the endoscope was immediately withdrawn without attempting to pass the stricture.

Age, gender, location of primary tumour, carcinoembryogenic antigen (normal if less than 10 ng/ml), ASA class [3], presence of metastatic disease in one or multiple organs, volume of liver metastases, urgency of the procedure and treatment with chemotherapy were evaluated in both groups. Data on morbidity, mortality, rate of stoma creation, hospital stay and compliance of chemotherapy were collected to compare results of both groups. Stent migration, need of a new endoscopic procedure or need of radiotherapy over primary tumour after 30 days of the initial procedure were considered long-term complications of the primary cancer. To establish the rate of liver tumour volume, we calculated the tumour volume measuring the diameter of the metastases seen on CT and the total liver volume using a previously described formula [4].

Since performance status and comorbidities may not permit an adequate chemotherapy regimen and, to get more homogeneous groups for analysis, both groups were subdivided into subgroups of patients suitable and unsuitable for ChT treatment.

Data were collected from a prospective database of the Department of General Surgery and clinical records.

Comparison of patient's characteristics was assessed by means of a chi-square test and a Mann–Whiney test. Differences of survival were evaluated by the log-rank test.

Results

There were 53 men and 45 women with a mean age of 71 (range, 45 to 94) years. Comparison of baselines characteristics of groups are summarized in Table 1. Both groups were comparable regarding age, ASA-class, ChT treatment, tumour location and presence of metastatic disease in one or multiple organs but not in gender and rate or urgent procedures. Moreover, group B showed a significantly higher rate of patients with increased CEA levels and of volume of liver metastases >25%.

Table 1 Baselines characteristics of surgical and endoscopic groups

Variable	Surgery, 53	Stent, 45	*p* value
Gender			
Male	29 (54.7)	38 (84.4)	0.002
Female	24 (45.3)	7 (15.5)	
Age (years)			
<75	35 (66)	26 (57.7)	0.403
>75	18 (34)	19 (42.2)	
CEA (ng/ml)			
<10	15 (31.9)	5 (11.9)	0.025
>10	32 (68.1)	37 (88)	
Unknown	6	3	
Procedure			
Urgent	24 (45.3)	10 (22.2)	0.017
Elective	29 (54.7)	35 (77.7)	
ASA class			
I	2 (4.5)	1 (5.2)	0.611
II	14 (31.8)	6 (31.5)	
III	21 (47.7)	11 (57.8)	
IV	7 (15.9)	1 (5.2)	
Unknown	9	26	
Tumour location			
Right colon	16 (30.2)	5 (11.1)	0.060
Left colon	23 (43.3)	24 (53.3)	
Rectum	14 (26.4)	16 (35.5)	
Metastatic lesion			
Single organ	40 (75.5)	31 (68.8)	0.511
Multiple organs	13 (24.5)	14 (31.1)	
Chemotherapy			
Yes	35 (66)	25 (55.5)	0.291
No	18 (34)	20 (44.5)	
Volume liver			
<25%	39 (88.6)	23 (63.8)	0.012
>25%	5 (11.3)	13 (36.1)	
Unknown	4	8	

In 44 of 53 operated patients (group A), primary tumour was resected (83%), with stoma creation (Hartmann procedure) in six patients (13.6%). Twelve of these 44 patients (27.2%) experienced medical or surgical complications, and five of them (11.3%) required further surgery due to anastomotic leak (n=2), perforation of right colon (n=1), retraction of stoma (n=1) and evisceration (n=1). One of these patients (2.2%) died. Other complications were wound infection (n=3), myocardial infarct, anaemia, ileus and respiratory failure. Primary tumour was not resected in nine patients, ending the operation with a lateral stoma in six cases (66.6%), a by-pass in one and as an exploratory laparotomy in two cases. Three of the unresected patients (33.3%) had complications; one patient (11.1%) needed further surgery due to stoma retraction and four patients (44.4%) died within 30 days. For unresected patients, median of survival was 3.6 months. Primary tumour resection provided significant benefit in survival (13.6 vs 3.6 months; p=.000). Table 3 shows post-procedure events.

Analyzing group B, 41 patients (91.2%) had a successful stent placement with obstruction relief. Four patients (8.8%) needed urgent surgery, two of these due to absence of intestinal obstruction relief and two after colonic perforation. In one of these patients (2.2%), a stoma was formed, and two patients (4.4%) died. No complication was observed in right side tumours.

Early complications were significantly rarer in group B, without a difference in related procedure mortality. Median hospital stay after SEMS placement was significantly shorter than after surgery. There was a remarkable significant difference in the rate of stoma creation, much lower after SEMS placement than after surgery (Table 2).

Median survival for the whole of patients was 9.8 months. Survival in group A was significantly higher (median, 11.9 months) than in group B (median, 7.3 months; log-rank test, P=.002; Fig. 1).

Table 3 shows baseline characteristics of the 60 patients who received ChT. Both subgroups, operated and palliated with a SEMS, were comparable regarding age, tumour location, ASA-class, presence of metastatic disease in one or multiple organs and volume of liver metastases >25%.

Statistically significant differences in gender, rate of urgent procedures and CEA levels were found. After surgical or endoscopic procedure, time to ChT was shorter in group B (46.9 vs 22.3 days; p=0.019). Late complications from the primary tumour were much more common in group B than in group A (5.71% vs 36%; p=0.000). In group B, seven patients (28%) needed some endoscopic procedure and in three, a new stent was inserted. In three patients, the stent was occluded due to faecal impaction and all of them could be successfully managed endoscopically. Stent migration occurred in two patients without the need of a new endoscopic procedure in one of these. Two patients in group A (without primary tumour resection) and one in group B needed radiotherapy for local pain. No patient needed surgery. Median survival was 12.5 months for

Table 2 Post-procedure outcomes of surgical and endoscopic groups

Variable	Surgery	Stent	*p* value
Early complications	15 (28.3%)	4 (8.8%)	0.011
Related procedure mortality	5 (9.4%)	2 (4.4%)	0.5
Stoma formed	13 (24.5%)	1 (2.2%)	0.003
Hospital stay (days)	14.8	4.8	0.003

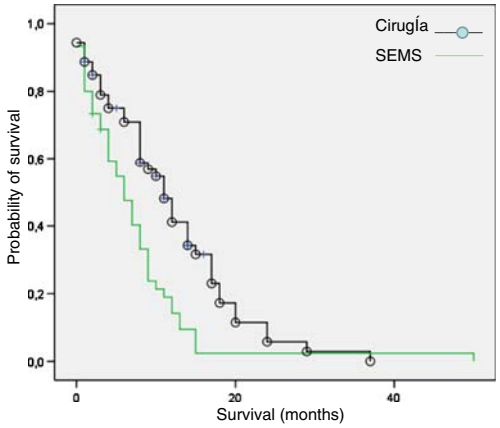

Fig. 1 Kaplan–Meier survival curves: Benefit in surgical group over SEMS for all group (p=0.002)

patients who received ChT, and there was a statistical difference between the two subgroups (median survival, 14.1 months for surgery vs 10 months for stent; log-rank test, p=0.023; Fig. 2).

For patients who did not receive ChT, median of survival was 5.2 months and there was no difference between the two subgroups (median survival, 6.8 months for surgery vs 3.9 months for stent; log-rank test, p=0.101; Fig. 3).

Discussion

Incurable stage IV colorectal cancer must be considered to include an heterogeneous group of patients, because incurability may be caused by non-resectable distant metastases, locally unresectable tumour growth that does

Table 3 Baselines characteristics and post-procedure events of surgical and endoscopic groups (QT)

Variable	Surgery, 35	Stent, 25	p value
Gender			
Male	20 (57.1)	20 (80)	0.06
Female	15 (42.8)	5 (20)	
Age (years)			
<75	28 (80)	18 (72)	0.47
>75	7 (20)	7 (28)	
CEA (ng/ml)			
<10	10 (28.5)	1 (4)	0.016
>10	25 (71.4)	24 (96)	
Unknown			
Procedure			
Urgent	14 (40)	4 (16)	0.047
Elective	21 (65)	21 (84)	
ASA class			
I	2 (6.4)	1 (7.6)	0.759
II	13 (41.9)	5 (38.4)	
III	12 (38.7)	7 (53.8)	
IV	4 (12.9)	0	
Unknow	4	12	
Tumour location			
Right colon	11 (31.4)	2 (8)	0.154
Left colon	15 (42.8)	14 (56)	
Rectum	9 (25.7)	9 (36)	
Metastatic lesion			
Single organ	25 (71.4)	15 (60)	0.41
Multiple organs	10 (28.5)	10 (40)	
Volume liver			
<25%	27 (84.3)32	11 (61.1)18	0.164
>25%	5 (15.6)	7 (38.8)	
Unknown	1	6	
Late complications of Primary tumour	2(5.7)	9 (36)	0.000
Time to chemotherapy(days)	46.9	22.3	0.019

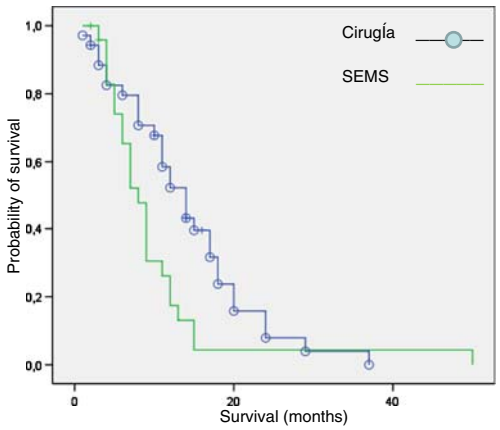

Fig. 2 Kaplan-Meier survival curves: Benefit in surgical group over SEMS for patients treated with ChT (p=0.023)

not allow surgery and comorbidities or poor performance status that do not permit surgery or ChT.

The best approach for patients with synchronous metastases of colorectal cancer is unclear. Chemotherapy might be the standard treatment for asymptomatic patients, who can be managed without primary tumour resection [5, 6]. Operative management is however necessary for patients with complications such as colonic obstruction. Since the purpose of these procedures is palliative, they ideally should offer low morbidity and mortality, a short hospital stay, to allow an early systemic therapy and a good compliance of treatment with ChT. In this setting, decision about surgery or SEMS placement is controversial. Some authors argued that tumour resection improves survival. Yun et al. [7] found benefit from resecting primary tumour, although in asymptomatic incurable disease only ChT influenced survival. In a recent review [8], tumour resection was related with a better survival and a lesser requirement of transfusions. On the other hand, no difference in survival was found between surgery and SEMS placement among other authors [9–13].

The deficiencies of a retrospective study are acknowledged. Selection bias can be appreciated in our study as shown in Table 2. Right colon tumours or in cases of emergency had a more tendency to surgery. Patients having

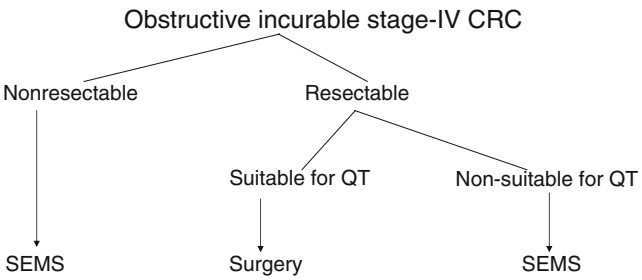

Fig. 3 Flow diagram of our proposal or treatment

more advanced disease (higher rate of increase in CEA and volume of liver replacement >25%) were more commonly stented. Both of these features have been related to survival [14, 15] and can have an influence in results. In our series, survival was higher in group A (11.9 months vs 7.3 months; p=.001) and these figures are comparable to others reports [8–12], with the only exception that stent placement has a tendency to a longer survival than surgery.

Ptok et al. found a more prolonged survival when primary tumour had been resected than when other surgical procedures were performed (17 vs 5.6 months) [12]. In our series, survival for patients in group A with primary tumour resection had benefit in survival (13.6 vs 3.6 months; p=.000). Moreover, since this unresected group of patients had a high rate of morbidity, mortality and stoma creation, we believe that, in the setting of obstructive incurable colorectal cancer, surgery without resection of primary tumour should be avoided whenever possible.

Lower rates of primary tumour resection in the surgical arm might explain the absence of benefit of surgery in other reports. In our study, primary tumour resection was performed in 44 patients (83%) in group A; this rate is higher than that reported by others and ranging between 47.6% and 66% [8, 9, 11].

Previous reports [9–13] have shown lower early morbidity and mortality rates and shorter hospital stay in stented patients, being comparable in our data. In group A, colostomy rate is much higher than in the stent group (24.5% vs 2.2%; p=.003). Some authors have reported higher rates of stoma creation, ranging between 46% to 63% [9, 11, 13]. Our relatively low rate can be related to a higher proportion of primary tumour resection and the inclusion of right colon cancer. Our complication rate in surgical arm (27%) is comparable with other reports, ranging between 26% to 53% [9–12]. In patients who received chemotherapy, time to chemotherapy administration was shorter in patients from group B (46.9 vs 22.3 days; p=.019).

Although SEMS placement may be expected to cause a low early morbidity rate, long-term complications have been described. Faragher et al. found delayed complications in nine of 25 patients (two needed surgery, three a second stent placement and four experienced stent migration) with a median time from stent insertion to failure of 14 months [11]. For Ptok et al. median in situ duration of the stent was 5.3 months and 11 of 38 patients (29%) suffered stent-related problems [12]. This fact may have an influence in compliance of ChT and in survival and, if a long survival is expected, stent insertion might not be the best option. In our series, long-term problems secondary to primary tumour occurred in 36% and 5.7% of patients of groups B and A who received chemotherapy.

In our study, patients from group A who received ChT had a benefit in survival (14.1 vs 10 months; $p=.023$). This result may be influenced by patient selection bias from a retrospective fashion of study, by absence of primary tumour complications and better compliance of ChT treatment.

In patients without ChT treatment, surgery did not provide any benefit in survival (6.8 vs 3.9 months; $p=.101$) in concordance with a previous report [12]. Since a short survival is expected, incidence of long-term complications from primary tumour is low and stent placement might be the best option for non-candidates to ChT. On the basis of these results, for patients of our multidisciplinary team, we propose the algorithm shows in the Fig. 3.

In conclusion, although SEMS placement offers advantages regarding early morbidity, hospital stay and stoma creation, long-term complications from primary tumour can be expected. Surgery offers a benefit in survival in patients who receive ChT but not in non-candidates to ChT. Surgery without primary tumour resection must be avoided when possible.

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