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ORIGINAL ARTICLE

Laparoscopic extended right colectomy versus laparoscopic left colectomy for carcinoma of the splenic flexure: a matched case–control study

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Abstract
Purpose The aim of the study was to compare the short- and long-term outcomes of laparoscopic extended right colectomy (ER) versus laparoscopic left colectomy (LC) for splenic flexure carcinomas.
Methods Patients with stage 0–III adenocarcinoma of the splenic flexure who underwent laparoscopy between 2000 and 2013 were identified from a prospectively maintained database. Twenty-seven patients who underwent ER were matched by age, gender, BMI, ASA score, and tumor stage with 27 patients who underwent LC.
Results The ER procedures were significantly longer than LC (235 ± 49.2 min vs. 192 ± 43.4 min, $p = 0.001$, respectively). Post-operatively, time to flatus and return to regular diet were observed to average 2.4 ± 0.8 days (1–4 days) and 4.6 ± 1.05 days (3–8 days), respectively, without differences between the groups. Overall, 14 complications were observed in 12 patients and 90-day mortality was nil. The length of hospitality stay was not different between ER and LC, with an overall mean of 8.3 ± 2.7 days. All procedures were classified as R0 resections, but ER was associated with a higher number of lymph nodes retrieved (21.4 ± 4.9) compared with LC (16.6 ± 5.5, $p = 0.001$). The 1-, 3-, and 5-year cumulative survival rates were 92.6, 85.8, and 72.8 % for the ER group and 96.3, 91.9, and 75.1 % for the LC group ($p = 0.851$). The 1-, 3-, and 5-year disease-free survival rates were 85.2, 76.7, and 67.1 % for the ER group and 96.2, 75.5, and 66.7 % for the LC group ($p = 0.636$).
Conclusions Laparoscopic ER and LC procedures performed for splenic flexure carcinomas appear to have similar short- and long-term oncologic outcomes.

Keywords Laparoscopy · Splenic flexure carcinoma · Extended right colectomy · Left colectomy

Introduction

European cancer statistics estimate that colorectal cancer (CRC) is the second most common tumor and the second most frequent cause of death from cancer, with 215,000 cases reported in 2012 [1–4]. Recent evidence supports that CRCs located at different sites, such as the right- or left-sided colon and rectum, have different histopathological appearance and different molecular and biological patterns [5–7], and therefore, they should be considered as distinct tumor entities [8]. In particular, colon carcinomas located at the splenic flexures (SFCs) are rather uncommon, accounting for 2–8 % of all CRCs treated by surgery [9–11]. SFCs are associated with a poorer prognosis compared to other colon cancers because they are generally found in more advanced stages [10], and they are associated with a higher risk of obstruction and lymphatic invasion [6, 10, 12]. However, a number of studies found no survival difference between left, right, and splenic flexure cancers after curative surgery [9–11].

The surgical management of SFCs is challenging because of the technical difficulties related to the peculiar dual

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lymphatic drainage of the superior and inferior mesenteric vessels, whose anatomy often shows heterogeneity [11, 13–16]. Moreover, the type of surgical resection, either via laparoscopy or open approach, in the case of SFCs is non-standardized. Although laparoscopy appears to be widely considered as safe and feasible [17, 18], the extent of the surgical resection remains arbitrary rather than evidence-based [19]. Some authors support more extensive resections, such as extended right colectomy with or without splenectomy and distal pancreatectomy, to assure the removal of all involved and potentially involved lymph nodes along the superior mesenteric vessels [12, 20]. On the opposite side, more conservative techniques, such as left hemicolectomy or segmental colectomy, have been advocated to avoid unnecessary resection of the middle colic artery [14–17]. However, the impact of extended surgery on the prognosis of SFC patients remains controversial [9, 12, 15].

The aim of the present study was to compare the short- and long-term oncologic outcomes of laparoscopic extended right colectomy (ER) versus laparoscopic left colectomy (LC) for SFCs.

Methods

Patient selection

After obtaining approval from the Institutional Review Board, patients' medical records were retrieved from a prospectively maintained database on colorectal cancers operated in the Unit of Digestive, Hepato-Pancreato-Biliary Surgery, and Liver Transplantation of the Henri Mondor Hospital in Créteil, France. We restricted the time period to patients who underwent surgery for CRC between January 2000 and January 2013. Of the 1184 procedures performed, we retrieved 93 patients operated on for adenocarcinoma of the splenic flexure. Of these, 68 were selected based on the following inclusion criteria: resectable tumor, primary anastomosis without stoma diversion, and surgical treatment by laparoscopic extended right colectomy or left hemicolectomy. Patients with locally advanced tumors adhering to or invading other organs or structures (T4b score) and those with obstructive tumors, metastatic disease (stage IV), or more than one carcinoma of the colon and polyposis coli were excluded. Moreover, only elective surgeries were considered for the analysis in the present study. To compare the two laparoscopic techniques, the ER and LC groups were matched, according to a 1:1 ratio, on age, gender, BMI, ASA score, and 0 to III tumor stage by American Joint Committee on Cancer (AJCC). After matching, 27 ER patients and 27 LC patients were finally included for the study analyses (Fig. 1).

Pre-operative workup

Tumor location was identified by colonoscopy and total body computed tomography with contrast enhancement. In case of suspected lymphatic packets, positron emission tomography (PET) with lymphatic biomarkers was performed for pre-operative staging. For small lesions, ink tattooing by colonoscopy was used 48 h before the surgical procedure. The decision to proceed with laparoscopy ER or LC was made on a patient-by-patient basis following discussion in a multidisciplinary meeting. Three surgeons operating in pairs with expertise in laparoscopic upper and lower gastrointestinal surgery performed all procedures. Prior to surgery, all patients underwent bowel preparation. They all received perioperative broad-spectrum parenteral antibiotics and subcutaneous low-molecular-weight heparin.

Surgical techniques

For both surgical techniques, the patient was placed in the classical Lloyd-Davis position with both arms along the body. Entry into the peritoneum was achieved by the Hasson's technique. Laparoscopic trocars were positioned as previously described for ER [21, 22] and LC [23, 24].

The ER procedure was defined as the resection of the right and transverse colon and a part of descending colon. The ileocolic, the right colic (if present), the middle colic, and the left colic arteries were ligated at their origins. The side-to-side anastomosis between the ileum and colon was performed with a mechanical stapler.

The LC procedures consisted of resection of the colonic segment between the left third of the transverse colon and the colorectal juncture. The inferior mesenteric artery and the left branch of the middle colic artery were ligated at their origin. End-to-end anastomosis was performed using a circular stapling device.

The removal of the lymph nodes from the root of the middle colic artery and the inferior mesenteric artery was routinely performed. All procedures were performed to achieve at least 5-cm proximal and distal tumor-free margins and tension-free anastomoses.

Adjuvant chemotherapy

Patients with stage III tumors or those with unfavorable histopathological characteristics underwent adjuvant chemotherapy unless contraindications related to the patient's performance status were present.

Short- and long-term outcomes

Patient demographic data, clinical presentation, operative parameters (e.g., operative time and blood loss), post-operative

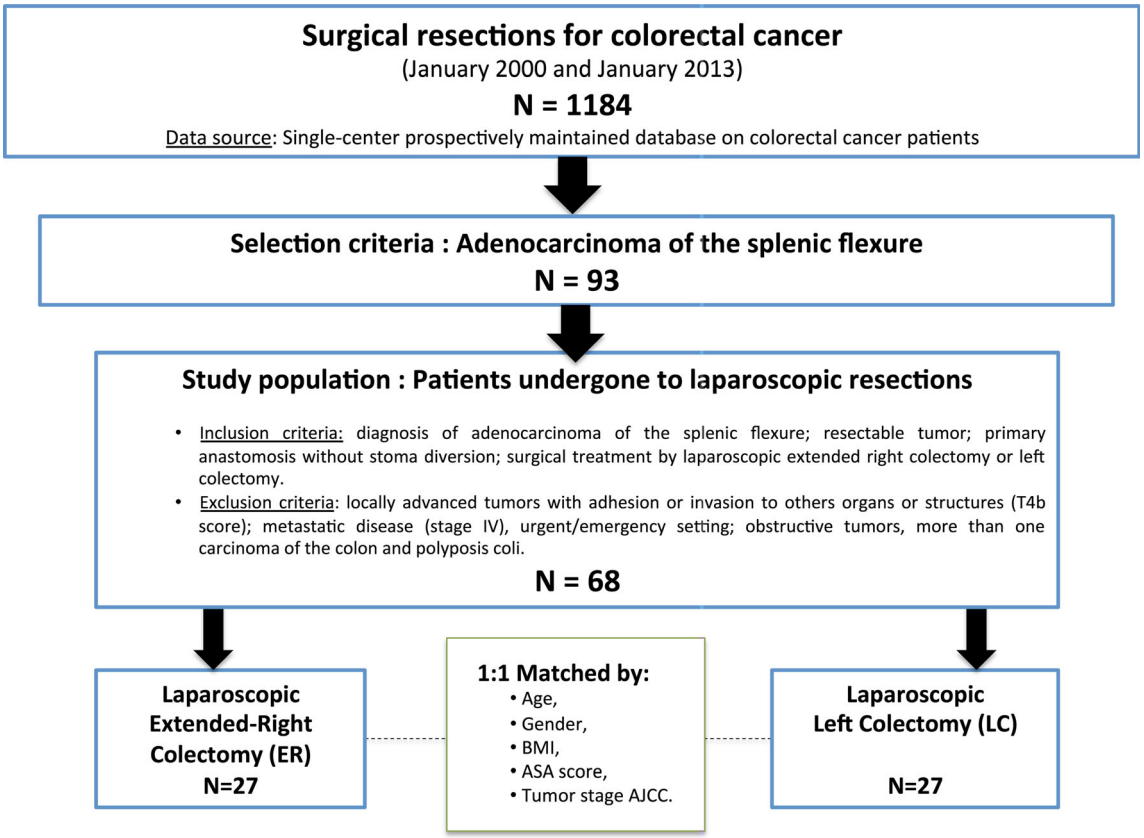

Fig. 1 Flowchart of patient selection and matching

variables (e.g., morbidity, time to flatus, and length of hospital stay), histopathological characteristics, and survival rates were analyzed.

Follow-up

All patients were followed every 3 months for the first 3 years and every 6 months thereafter (French Guidelines from the Thesaurus National de Cancerologie Digestive, 2011). At the follow-up visits, physical examination, computed tomography, and serum chemistry analysis were performed. Colonoscopy was generally performed if abnormalities were detected during any follow-up visit.

Statistical analysis

For bivariate two-sided comparisons between the ER and the LC groups, the chi-squared test or Fisher's exact test was used for categorical variables, and according to the data distribution, the *T* test or Mann-Whitney *U* test was applied for continuous variables. Hence, continuous data were expressed as means (standard deviation, SD) or medians and ranges (minimum to maximum). Overall and disease-free survivals were analyzed using the Kaplan-Meier method. Survival curves were compared using the log rank (Mantel-Cox) test. A p value <0.05 was considered to be statistically significant. Statistical analyses were performed with SPSS (Statistical Package for Social Science, IBM SPSS Statistics, version 22 for Macintosh).

Results

The demographic and clinical characteristics of patients in the ER and LC groups are summarized in Table 1. No group difference was noted for pre-operative hemoglobin, leukocytes, albumin level, weight loss (>10 % of ideal body weight), and comorbidities.

Operatively, the two laparoscopic techniques did not differ significantly, except for the duration of the operation, which was significantly shorter for the LC procedures ($p = 0.001$). Conversion to laparotomy was necessary only in one patient in the ER group due to uncontrolled hemorrhage on the right colic vessel pedicule following technical problems with the mechanical vascular stapler. However, the post-operative outcome of this patient was uneventful (Table 2).

Post-operatively, the time to flatus and the return to regular diet in the ER and LC groups were observed in an average of 2.4 ± 0.8 days (range 1–4 days) and 4.6 ± 1.05 days (range 3–8 days), respectively, without difference between groups.

Table 1 Demographic data and clinical characteristics of patients treated by laparoscopic extended right colectomy (ER) or left colectomy (LC) for splenic flexure cancer

Variables	ER ($n=27$)	LC ($n=27$)	P value
Gender (F/M) [n]	8/19	8/19	1
Age (year) [mean (SD)]	66.8 (9.3)	65.5 (10)	0.585
BMI (kg/m^2) [mean (SD)]	24.7 (4.3)	24.5 (3.4)	0.853
Pre-operative hemoglobin (g/L) [mean (SD)]	13.1 (1.9)	12.3 (1.8)	0.127
Pre-operative leukocytes (10^9/L) [mean (SD)]	7.88 (2.34)	7.95 (2.52)	0.911
Albumin serum level (g/L) [mean (SD)]	37.38 (5.6)	38.3 (5.3)	0.533
Weight loss (>10 %) [n (%)]	4 (14.8)	3 (7.4)	0.669
Kidney failure [n (%)]	0	1 (3.7)	1
Diabetes [n (%)]	4 (14.8)	2 (7.4)	0.669
Cardiovascular diseases [n (%)]	9 (33.3)	12 (44.4)	0.577
Pulmonary disease [n (%)]	1 (3.7)	2 (7.4)	1
ASA score [n (%)]			1
I	11 (40.7)	11 (40.7)	
II	12 (44.4)	12 (44.4)	
III	4 (14.8)	4 (14.8)	
IV	0	0	
TNM AJCC stage[a] [n (%)]			1
0	1 (3.7)	1 (3.7)	
I	3 (11.1)	3 (11.1)	
II	6 (22.2)	6 (22.2)	
III	17 (63)	17 (63)	
Chemotherapy [n (%)]			1
None	12 (44.4)	11 (40.7)	
Adjuvant	15 (55.6)	16 (59.3)	

BMI stands for body mass index; *ASA* for American Society of Anesthesiology; *TNM* for tumor, nodes, and metastasis score; and *AJCC* for American Joint Committee on Cancer

[a] In the TNM AJCC categories II and III, the subcategories including T4b tumors (i.e., tumors directly invading or adherent to other organs or structures) were not included

Overall, 14 complications were observed in 12 patients. No reintervention was needed; all complications were resolved by conservative treatments. Mortality within 90 days was nil. The length of hospitality stay was not different between ER and LC, with an overall average of 8.3 ± 2.7 days (range 5–24). Six patients (five in the ER group and one in the LC group) were readmitted within 30 days from surgery due to urinary infections (1), wound infection (3), abnormal bowel transit (1), and hematochezia (1) (Table 2), which were medically treated.

All ER and LC procedures were classified as R0 resections (Table 3). In the majority of the patients (87 %), more than 12 lymph nodes were harvested during the colonic resection, without difference between groups. However, a significantly higher number of lymph nodes were retrieved in the ER procedures (mean 21.4 ± 4.9) than in the LC procedures (mean 16.6 ± 5.5) ($p=0.001$). In the 34 patients classified as TNM AJCC stage III, no metastasis was observed in the lymph nodes retrieved along the superior mesenteric vessels during the ER procedures or along the root of the middle colic artery during the LC procedures. Tumor size and grade of differentiation did not differ between groups (Table 3).

During the follow-up (overall mean follow-up 70.9 months (SD 46.1)), eight patients (29.6 %) in the ER group and six patients (22.2 %) in the LC group had tumor recurrence ($p=0.757$). These were five (18.5 %) hematogenous metastases and three (11.1 %) seeding in the ER and five (18.5 %) hematogenous metastases and one (3.7 %) lymph node metastasis in the LC.

Cumulative survival and disease-free survival at 1-, 3-, and 5-year post-surgery were not different between groups. As shown in the survival curves (Figs. 2 and 3), the 1-, 3-, and 5-year cumulative survival rates were 92.6, 85.8, and 72.8 % for the ER group and 96.3, 91.9, and 75.1 % for the LC group ($p=0.851$). The 1-, 3-, and 5-year disease-free survival rates were 85.2, 76.7, and 67.1 % for the ER group and 96.2, 75.5, and 66.7 % for the LC group ($p=0.636$).

Discussion

The present study focused on the laparoscopic management of SFC. As previously described, laparoscopy is safe and

Table 2 Short-term outcomes of patients treated by laparoscopic extended right colectomy (ER) or left colectomy (LC) for splenic flexure cancer

Variables	ER ($n=27$)	LC ($n=27$)	P value
Operative time (min) [mean (SD and range)]	235 (49.18) (160–360)	192.2 (43.4) (120–280)	0.001
Conversion to laparotomy [n (%)]	1 (3.7)	0	1
Operative blood loss (mL) [mean (SD)]	120 (43.5)	110 (45.1)	0.411
Number of transfused patient [n (%)]	1 (3.7)	0	1
Time to flatus [mean (SD and range)]	2.5 (0.75) (1–4)	2.3 (0.87) (1–4)	0.406
Return to regular diet [mean (SD and range)]	4.6 (0.84) (3–7)	4.6 (1.2) (3–8)	1
Post-operative complications [n (%)]			0.745
Ileus	0	2 (7.4)	
Anastomotic leakage	1 (3.7)	0	
Intra-abdominal abscess	2 (7.4)	1 (3.7)	
Wound infection	2 (7.4)	4 (14.7)	
Pancreatic fistula	1 (3.7)	1 (3.7)	
Intestinal bleeding	0	0	
Dindo-Clavien classification [n (%)]			0.801
I	5 (18.5)	4 (14.8)	
II	1 (3.7)	2 (7.4)	
Mortality within 90 days [n]	0	0	NA
Length of hospital stay (days) [mean (SD and range)]	8.6 (3.4) (6–24)	8.1 (1.8) (5–14)	0.852
Readmission within 60 days [n (%)]	5 (18.5)	1 (3.7)	0.192

feasible with the advantages of lower blood loss and shorter recovery compared to open surgery [17, 21, 25–27]. In recent years, with advances in minimally invasive surgery experience, the laparoscopic approach might be considered the standard of care; however, the selection of the most appropriate laparoscopic operative procedure in case of SFC remains a matter of debate [19].

The present study shows that laparoscopic ER and LC resections have similar short- and long-term outcomes in patients with resectable SFC without metastatic disease. In all these selected patients, an R0 resection with adequate tumor-free margins and number of lymph nodes harvested was achieved regardless of the type of laparoscopic technique performed. The achievement of the entire tumor area resection with adequate margins and lymph nodes is considered challenging in case of SFCs [28], because the blood supply of this colonic segment has been shown to vary between patients. An early study by Griffith [29] reported that blood supply to the splenic flexure is carried by the inferior mesenteric artery via the left colic artery in the majority of cases, but in a considerable number of patients, estimated at 11 %, this is carried by the superior mesenteric artery via the left branches of the middle colic artery [29]. In consequence, the surgical management of lymph nodes may be inappropriate or suboptimal if the different anatomies are not taken into account. Over the years, extended resections have been recommended to overcome the

Table 3 Histologic findings in patients treated by laparoscopic extended right colectomy (ER) or left colectomy (LC) for splenic flexure cancer

Variables	ER ($n=27$)	LC ($n=27$)	P value
R0 resection [n (%)]	27 (100)	27 (100)	NA
Number of lymph nodes harvested [n (%)]			0.420
<12 lymph nodes	2 (7.4)	5 (18.5)	
≥12 lymph nodes	25 (91.6)	22 (82.5)	
Tumor size maximum diameter (cm) [mean (SD and range)]	5.8 (2.9) (3–14)	5.3 (1.9) (3–12)	0.931
Adenocarcinoma [n (%)]			0.382
Well differentiated	18 (66.7)	16 (59.3)	
Moderately differentiated	5 (18.5)	9 (33.4)	
Mucinous	4 (14.8)	2 (7.4)	

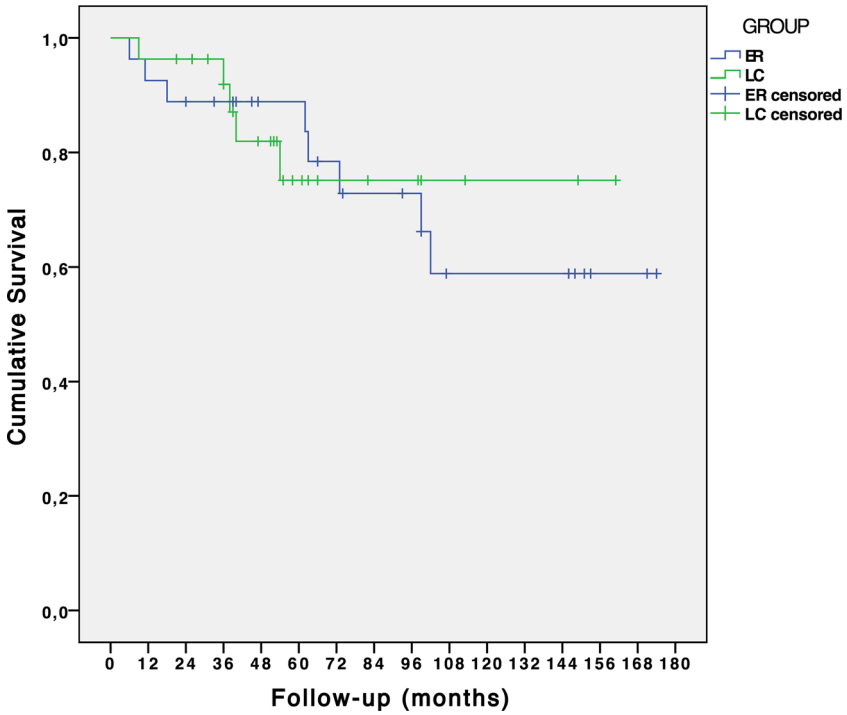

Fig. 2 Overall survival curves (Kaplan-Meier) for patients treated by laparoscopic extended right colectomy (ER) or left colectomy (LC) for splenic flexure cancer

poor oncologic outcomes observed in patients with SFCs [12, 20]. However, some studies demonstrated that SFCs are not associated with a worse prognosis even when treated by left partial colectomy [9, 11, 15]. Moreover, histological examinations revealed that the majority of lymph nodes metastases are located along the paracolic arcade and the left colic artery [15], while other reports support the presence of positive lymph nodes at the root of the middle colic artery and superior mesenteric artery [20, 30]. The present study found no positive lymph nodes along the superior mesenteric artery confirming the rarity of metastases in this location for SFCs. Therefore, the rationale for extensive resections appears to fade in front of comparable R0 margin rate and oncologic outcomes between ER and LC. However, some recent

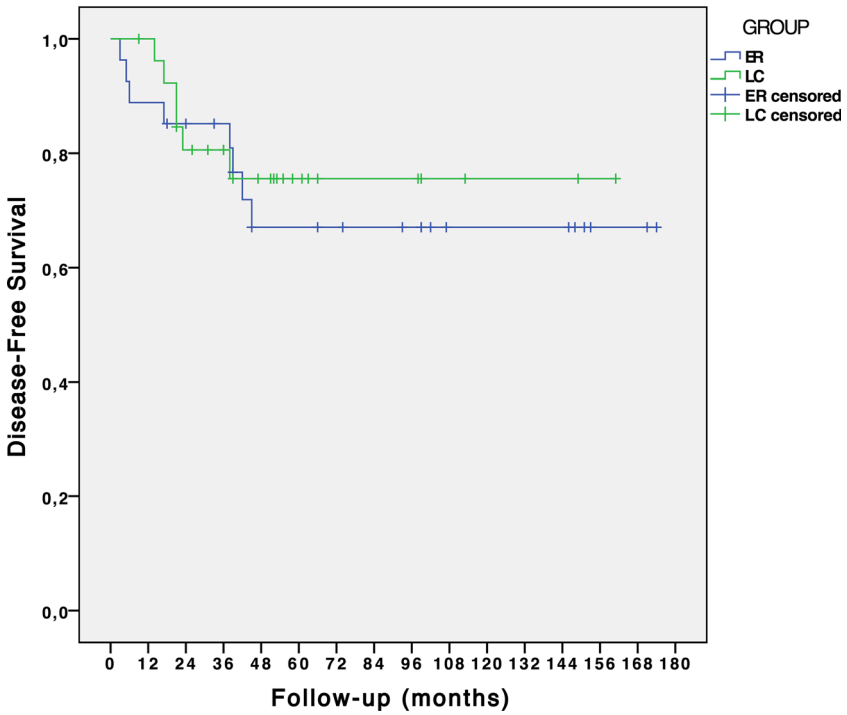

Fig. 3 Disease-free survival curves (Kaplan-Meier) for patients treated by laparoscopic extended right colectomy (ER) or left colectomy (LC) for splenic flexure cancer

evidence supports the theoretical importance of extra-mesocolic lymph nodes as potential metastatic routes of carcinomas of the transverse colon and of both flexures, which deserve more attention in future studies aimed to assess the adequate extension of lymph node regional dissection in ER and LC procedures [31].

As recommended, a minimum of 12 lymph nodes is commonly accepted for correct tumor staging [32], even if it is always desirable to examine as many nodes as possible [33, 34]. Although in the majority of the patients that underwent ER and LC more than 12 lymph nodes were harvested and analyzed, a greater number of lymph nodes were retrieved by performing ER resections. This was expected due to the proportion of the extension of the ER procedure, which requires the ligation and resection of at least three colonic vascular pedicles. However, this appeared to have no impact on the overall and disease-free survival rates, which may depend not only on the lymph node count but also on the ratio and location of the involved lymph nodes [35].

In contrast to other series [16], no local recurrence was observed in the present study. This may be related to the exclusion from this analysis of locally advanced tumors (stage T4b) and to the achievement of R0 resection in all cases. It is noteworthy that all procedures were carried out in elective settings by experienced colorectal surgeons, who were able to manage the technical challenges of performing ER and LC resections by laparoscopy, as demonstrated by the low rates of intra-operative complications and conversion to laparotomy. As reported in other studies [10, 11], the observed recurrences were only systemic spread of SFC that appears to not behave differently than other colonic cancers.

Overall and disease-free survival rates were not different in the ER and LC groups. The observed rates are in accordance with those previously reported in the literature, with trends toward better survivals in our series [11, 15, 16]. However, it must be considered that obstructive tumors and emergencies, which are known to be negative predictors of patient survival [30, 36, 37], have been excluded from the analysis.

The present study has some limitations mainly related to its retrospective nature and the relative small number of patients included. The study spans over a long time frame, and thus, historical bias cannot be excluded. However, this study focuses on a particular and rather uncommon subtype of colorectal cancer, i.e., SFC, which has been rarely investigated.

Conclusion

In conclusion, these findings support both laparoscopic extended right and left colectomy as curative surgeries for SFCs, which are associated with similar short- and long-term oncologic outcomes. However, further prospective and multicentric clinical trials, assessing both clinical and patient's centered outcomes (e.g., quality of life), are awaited to provide evidence-based selection criteria of the most appropriate surgical approach.

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