



ORIGINAL ARTICLE

Laparoscopic versus open surgery for left flexure colon cancer: A propensity score matched analysis from an international cohort

Corrado Pedrazzani¹ | Giulia Turri¹ | Soo Yeun Park² | Koya Hida³ |
 Yudai Fukui³ | Jacopo Crippa⁴ | Giovanni Ferrari⁵ | Matteo Origi⁵ |
 Gaya Spolverato⁶ | Matteo Zuin⁶ | Sung Uk Bae⁷ | Seong Kyu Baek⁷ |
 Andrea Costanzi⁸ | Dario Maggioni⁸ | Gyung Mo Son⁹ | Andrea Scala¹⁰ |
 Timothy Rockall¹⁰ | David W. Larson⁴ | Alfredo Guglielmi¹ | Gyu Seog Choi²

¹Division of General and Hepatobiliary Surgery, Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, University of Verona, Verona, Italy

²Colorectal Cancer Centre, Kyungpook National University Medical Centre, School of Medicine, Kyungpook National University, Daegu, Korea

³Department of Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan

⁴Division of Colon and Rectal Surgery, Department of Surgery, Mayo Clinic, Rochester, Minnesota, USA

⁵Department of General Surgery, Niguarda Hospital, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

⁶First Surgical Clinic Section, Department of Surgery, Oncology, and Gastroenterology, University of Padova, Padova, Italy

⁷Division of Colorectal Surgery, Department of Surgery, School of Medicine, Keimyung University and Dongsan Medical Centre, Daegu, Korea

⁸General Surgery 3, ASST-Monza, Desio Hospital, Desio, Italy

⁹Department of Surgery, Pusan National University Yangsan Hospital, School of Medicine, Pusan National University, Yangsan, Korea

¹⁰Department of Colorectal and Minimal Access Surgery, Royal Surrey NHS Foundation Trust, Guildford, UK

Correspondence

Corrado Pedrazzani, Division of General and Hepatobiliary Surgery, Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, Verona University Hospital, Piazzale L. Scuro 10, 37134 Verona, Italy.
 Email: corrado.pedrazzani@univr.it

Funding information

None.

Abstract

Aim: Surgical treatment of splenic flexure cancer (SFC) still presents some debated issues, including the role of laparoscopic surgery. The literature is based on small single-centre series, while randomized controlled studies comparing open and laparoscopic treatment for colon cancer exclude SFC. This study aimed to determine the role of laparoscopic surgery in the treatment of SFC, comparing short- and long-term outcomes with open surgery.

Method: This was an international multicentre retrospective cohort study that analysed patients from 10 tertiary referral centres. From a cohort of 641 cases, 484 patients with Stage I–III SFC submitted to elective surgery with curative intent were selected. After 1:1 propensity score matching, 130 patients in the laparoscopic group (LapGroup) were compared with 130 patients in the open surgery group (OpenGroup).

Results: After propensity score matching, the two groups were comparable for demographic and clinical parameters. OpenGroup presented a higher incidence of overall ($P = 0.02$) and surgery-related complications ($P = 0.05$) but a similar rate of severe complications ($P = 0.75$). Length of stay was notably shorter in the LapGroup ($P = 0.001$).

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2021 The Authors. *Colorectal Disease* published by John Wiley & Sons Ltd on behalf of Association of Coloproctology of Great Britain and Ireland

Overall ($P = 0.793$) as well as cancer-specific survival ($P = 0.63$) did not differ between the two groups.

Conclusions: Elective laparoscopic surgery for Stage I–III SFC is feasible and associated with improved short-term postoperative outcomes compared to open surgery. Moreover, laparoscopic surgery appears to provide excellent long-term cancer outcomes.

KEYWORDS

colon cancer, laparoscopy, left flexure, prognosis, splenic flexure

INTRODUCTION

Colorectal cancer (CRC) is one of the most frequent solid tumours worldwide but seldom arises at the splenic flexure [1]. Most commonly, cancers of the splenic flexure (SFCs) are defined as those located within the last third of the transverse colon, the splenic flexure itself, and the first 10 cm of the descending colon [2,3]. As described in a previous work from our group [1] and historical literature [3–6], SFCs are associated with negative prognostic factors such as higher risk of presentation with obstruction [6,7], advanced stage [8] and unfavourable mucinous histology [1,3,5]. Nonetheless, our data contradict the widely held dogma that SFC is associated with worse prognosis compared to other cancer sites [1].

Several randomized controlled trials demonstrated the non-inferiority of laparoscopy for colon cancer in terms of oncological outcome and its association with better short-term results [9–12]. SFCs were excluded from these trials due to their unfavourable clinical characteristics and lack of standardized surgical technique. Few data on the feasibility and outcomes of laparoscopy for SFC are currently available in the literature, mainly from single-centre series with a small number of patients [13–22].

The purpose of the study was to evaluate short- and long-term results of SFCs treated with laparoscopy compared to open surgery. Data from a large multicentre cohort were analysed after controlling for preoperative variables through propensity score matching (PSM).

MATERIALS AND METHODS

The study protocol was approved by the institutional review board and ethics committee of each of the 10 centres involved. From 21 338 patients, 641 consecutive patients (3%) with SFC were identified as previously described in detail [1]. Briefly, SFCs were retrospectively identified through review of preoperative colonoscopies, CT scans, operative reports and histopathology reports at each participating centre as those tumours located between the distal third of the transverse colon and the first 10 cm of the descending colon. All consecutive cases were included. To evaluate outcomes of laparoscopy compared to open surgery, we conducted a subgroup analysis of the global cohort considering patients who had surgery

What does this paper add to the literature?

Laparoscopy for colon cancer is widely accepted, although little evidence supports its use in the case of tumours located at the splenic flexure. This is the largest multicentre study confirming the feasibility of laparoscopy compared to open surgery for this location in terms of improved short-term outcomes and comparable long-term prognosis.

between January 2005 and December 2017. Patients were included if they underwent elective, potentially curative (RO–1) resection for Stage I–III SFC.

Outcome measures

Each centre retrieved relevant information from their institutional database. Clinical-pathological data, intra-operative data, postoperative mortality and morbidity, and oncological outcomes were compared between patients who underwent laparoscopic (LapGroup) and open surgery (OpenGroup). Analysis was performed on an intention-to-treat basis considering patients needing conversion to open surgery as laparoscopic cases. Completion of laparoscopic dissection was judged necessary to classify a procedure as laparoscopic. Conversion was defined as an inability to complete all intended laparoscopic steps laparoscopically. Anastomosis in the LapGroup was performed intracorporeally or extracorporeally depending on the surgeon's choice. All patients completed a documented follow-up of at least 24 months. Outcome measures were postoperative course, postoperative length of stay (LOS), overall survival (OS), cancer-specific survival (CSS) and recurrence pattern. Disease recurrence was defined as systemic, locoregional or peritoneal and was proved by radiological and/or pathological methods when available. Complications were graded according to the Clavien–Dindo classification [23] and divided into minor (Grade I–II) and major (Grade III–V). When several adverse events occurred in the same patient, the highest grade was considered.



Surgical technique

Over the study period, patients underwent laparoscopic or open resection according to surgeons' preference and experience. None of the surgeons at the participating centres was in their learning curve phase. Surgical interventions were classified based on the extent of colonic resection and vessel ligation level as previously described [1]. Common definitions were shared among participating centres to standardize surgical reports. Subtotal colectomy was defined as the resection of the terminal ileum, caecum, ascending and transverse colon, left flexure and descending colon, in which ileocolic, right colic, middle colic and left colic vessels were ligated. Left hemicolectomy entailed the resection of part of the transverse colon, descending colon and sigmoid colon with ligation of the inferior mesenteric vessels and the left branch of the middle colic vessels. Left high colectomy was defined as the resection of the distal transverse colon, left flexure and descending colon, with ligation of the left colic and the left branch of the middle colic vessels. For study purposes, left hemicolectomy and left high colectomy were considered together and named left colonic resection. Partial resection was defined as removing a portion of the colon without ligation of the primary vascular pedicles [24].

Statistical analysis

Continuous data were reported as mean (\pm SD) or median (interquartile range, IQR) as appropriate according to distribution, while categorical data were reported as frequencies and percentages. The ANOVA or Kruskal–Wallis test for continuous variables and chi-squared or Fisher's exact test for categorical variables were made by comparison between groups.

Adjusting potential confounding factors influencing the allocation of cases to the LapGroup rather than the OpenGroup, the PSM technique was applied. Multivariate logistic regression generated propensity scores, predicting the probability of undergoing laparoscopic surgery based on the variables which could influence surgical approach: centre (east vs. west), year of surgery (2005–2008 vs. 2009–2012 vs. 2013–2017), gender, age, body mass index, Charlson comorbidity index, previous abdominal surgery (yes vs. no), extra parietal tumour invasion ($pT < 4$ vs. $pT4$) and extent of surgery (subtotal colectomy vs. left colectomy vs. partial resection). Patients in the LapGroup were matched 1:1 with patients in the OpenGroup using the nearest neighbour method considering a caliper < 0.2 . After PSM was performed, differences between the two groups were assessed. Absolute standardized mean differences were estimated to evaluate post-match imbalance, and a standardized mean difference < 0.15 was considered a negligible difference in the mean or prevalence of a covariate between treatment groups. Table S1 reports standardized mean differences for matching variables before and after matching. The PSM adequacy was visually assessed by the frequency of propensity scores in each group before and after matching (Figure S1), and the overall balance test result was reported as a quantitative measure of balance. The overall balance test for the model used gave $d^2 = 7.527$ on 13 degrees of freedom ($P = 0.873$) confirming good balancing after PSM.

Overall survival and CSS were computed using the Kaplan–Meier method and compared using the log-rank test. Time of survival was calculated from the date of surgery to the most recent follow-up examination or death. CSS was measured from the date of surgery to the date of death from colon cancer, whilst patients who died from causes other than cancer were considered censored at the time of death. Multivariate analysis for OS and CSS was performed using the Cox regression model considering surgical approach (LapGroup vs. OpenGroup) and adjusting for the following risk factors: age (≥ 70 years old vs. < 70 years old), gender (male vs. female), grading (G1–2 vs. G3), extent of surgery (subtotal colectomy and partial resection vs. left colonic resection), TNM stage (Stage I and Stage II vs. Stage III) and administration of adjuvant chemotherapy (yes vs. no). All statistical tests were two-sided, and a P value lower than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 23.0 software (IBM Corporation, Armonk, New York, USA).

RESULTS

Patient selection

A minimally invasive approach was adopted in 341 patients (53.2%), while an open approach was preferred in 300 (46.8%). After applying exclusion criteria, 194 patients in the OpenGroup (64.7%) and 290 in the LapGroup (85%) were included for analysis. The selection process and the causes for exclusion are detailed in Figure 1. Following PSM, the final study population consisted of 260 patients, 130 patients who underwent laparoscopic resection and 130 patients who underwent open surgery.

Study population

Before PSM (Table S2), patients in the OpenGroup were significantly older (mean age \pm SD 69.8 ± 12.8 years old vs. 66.9 ± 11.4 years old; $P = 0.002$), presented a higher median Charlson comorbidity index score (3 [IQR 2–5] vs. 2 [IQR 2–3]; $P = 0.01$) and a higher rate of previous abdominal surgeries (33.5% vs. 23.4%; $P = 0.02$). Finally, tumours in the OpenGroup were more frequently obstructing (30.4% vs. 18.6%, $P < 0.001$) and locally advanced ($pT4$, 21.6% vs. 8.6%, $P < 0.001$). After PSM, the two groups were comparable as for demographic and clinical parameters (Table 1). From here on, the analysis will refer only to the matched cohort. Analysis of the operative data and short-term outcomes of the unmatched groups are available in Tables S3 and S4).

Operative data

Operative data and specimen characteristics are reported in Table 2. Eleven patients (8.5%) in the LapGroup needed conversion to open surgery. The most performed procedure was left colonic resection

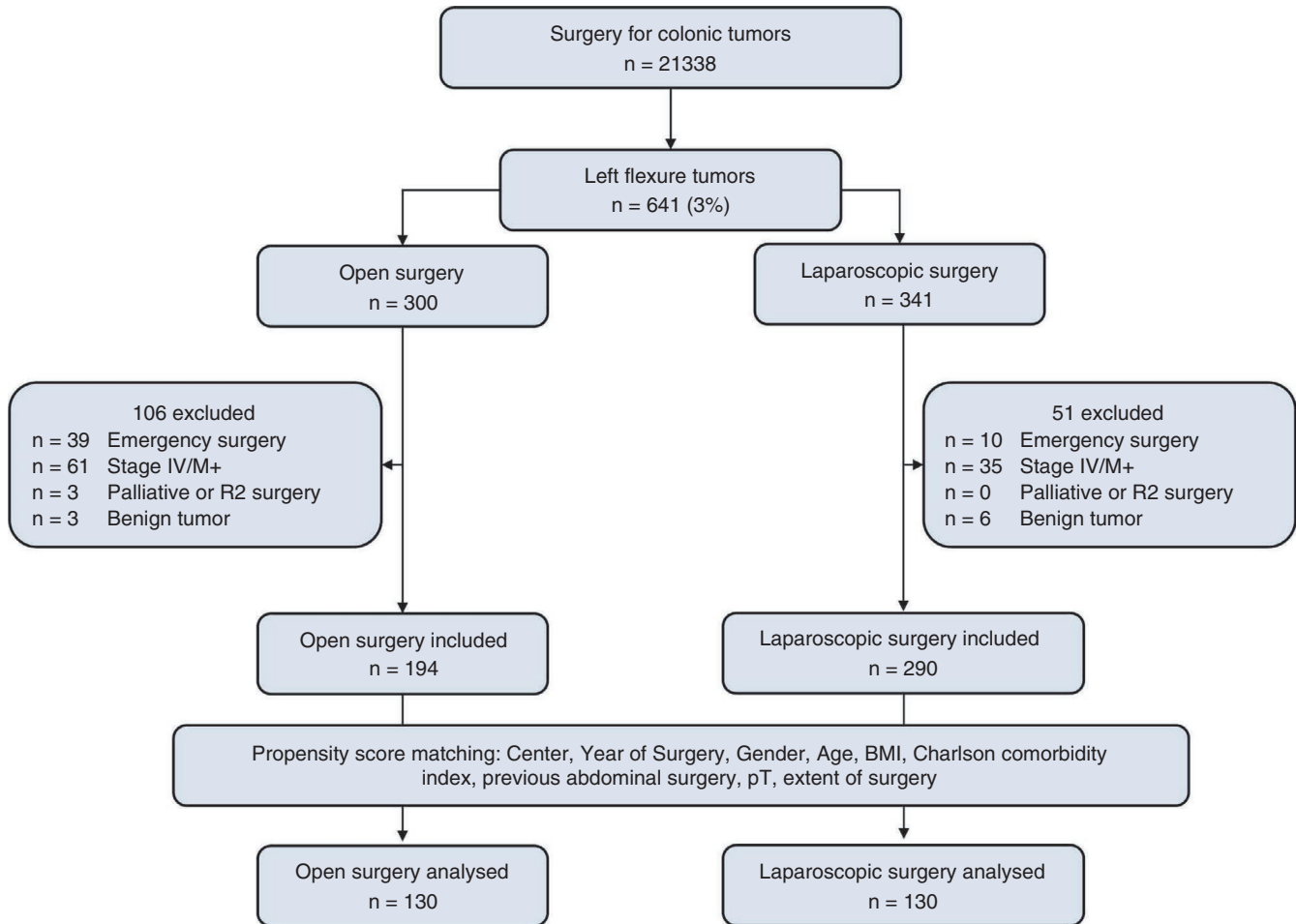


FIGURE 1 CONSORT flow diagram with patients' selection process, according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines

in both groups (83 cases in the LapGroup vs. 84 in the OpenGroup; $P = 0.68$), followed by partial resection of the splenic flexure (32 cases in the LapGroup vs. 35 in the OpenGroup). A similar proportion of patients in both groups needed resection of adjacent organs due to suspected tumour infiltration (seven patients in the LapGroup and 12 in the OpenGroup; $P = 0.34$). No patient in either group presented microscopic residual (R1) tumour on surgical resection margins. Specimen characteristics were comparable except for the median number of retrieved lymph nodes, which was lower in the OpenGroup (15 [IQR 11–21] vs. 17.5 [IQR 12–25]; $P = 0.01$). Similarly, a higher percentage of cases with less than 12 nodes was found in the OpenGroup (28.9% vs. 15%; $P = 0.03$).

Short-term outcomes

Patients in the OpenGroup (Table 3) presented a higher incidence of overall (33.1% vs. 17.7%; $P = 0.02$) and surgery-related complications (24.6% vs. 14.6%; $P = 0.05$), with a similar rate of severe complications (6.9% vs. 5.4%; $P = 0.75$). Regarding surgical complications, no difference was highlighted for anastomotic leak (2.3% vs.

1.5%; $P = 1$). Prolonged postoperative ileus (10% vs. 3.8%; $P = 0.08$) and surgical site infections (6.2% vs. 1.5%; $P = 0.10$) occurred more frequently after open surgery, but the difference did not reach statistical significance. As expected, LOS of the LapGroup was notably shorter than for the OpenGroup (median 7 days [IQR 5–10] vs. 9 days [IQR 7–15]; $P = 0.001$). Thirty-day mortality, redo surgery and readmission rates were similar between the two groups. The rate of administration of adjuvant chemotherapy was comparable in the two groups (22.2% in the LapGroup vs. 20.5% in the OpenGroup; $P = 0.87$).

Overall and cancer-specific survival

At the time of analysis, 135 patients (51.9%) completed 5 years of follow-up, with 57 suffering mortality (21.9%). The median length (IQR) of follow-up was 59.9 (37–98) months (61.3 [45–97.7] months for surviving patients) in the LapGroup and 60 (38–98) months (64.1 [47–107.3] months for surviving patients) in the OpenGroup ($P = 0.239$). As illustrated in Figure 2, OS in the whole cohort did not differ between open and laparoscopic surgery (5 years OS 81.4% vs.

TABLE 1 Patients' demographic and clinical data according to surgical approach after propensity score matching

	LapGroup (n = 130)	OpenGroup (n = 130)	P
Age, years, mean (SD)	67 (12.3)	69.5 (12.2)	0.09
Gender, men	68 (52.3)	73 (56.2)	0.62
BMI, kg/m ² , median (IQR)	23.9 (21.2–26.8)	23.7 (20.7–27.2)	0.45
Charlson comorbidity index, median (IQR)	2 (2–3)	2 (2–3)	1
Previous surgery	37 (28.5)	36 (27.7)	1
Presence of stenosis	27 (20.8)	34 (26.3)	0.09
Missing	7 (5.7)	15 (10.9)	
Depth of tumour invasion (pT)			0.91
pT1–2	34 (26.8)	36 (27.6)	
pT3	77 (60.6)	77 (60.6)	
pT4	16 (12.6)	14 (11)	
Missing	3 (2.3)	3 (2.3)	
Nodal involvement (pN)			0.84
pN0	93 (71.5)	97 (74.6)	
pN1	25 (19.2)	23 (17.7)	
pN2	12 (9.2)	10 (7.7)	
AJCC TNM stage			0.77
Stage I	31 (23.8)	32 (24.6)	
Stage II	63 (48.5)	67 (51.5)	
Stage III	36 (27.7)	31 (23.8)	
Mucinous histology	11 (8.5)	9 (6.9)	0.69
Poorly differentiated grading (G3)	21 (16.9)	19 (15.3)	0.86

Note: Values in parentheses are percentages unless differently specified.

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, body mass index; IQR, interquartile range.

85%, respectively; $P = 0.793$) although it was slightly better in the latter. Subgroup analysis according to stage showed similar results ($P = 0.263$ for Stage I, $P = 0.428$ for Stage II, $P = 0.439$ for Stage III). Considering CSS, patients showed comparable survival rates after open and laparoscopic surgery ($P = 0.63$, Figure 3), and the result was confirmed at subgroup analysis for stage. Multivariate analyses for OS and CSS were conducted considering surgical approach and adjusting for other relevant risk factors (Table 4). Laparoscopy did not prove to be an independent prognostic factor for OS or CSS ($P = 0.72$).

Disease recurrence

Recurrence developed with similar rates in the two groups, 19 patients (14.6%) in the LapGroup and 18 patients (13.8%) in the OpenGroup ($P = 1$). Systemic recurrence in the form of hepatic relapse was found in 13 patients (10%) in the OpenGroup and eight patients (6.2%) in the LapGroup ($P = 0.36$). Patients in the laparoscopic cohort developed peritoneal and locoregional recurrence more frequently than after open surgery (3.1% vs. 0%, and 2.3% vs. 0.8%, respectively), but the difference did not reach statistical significance.

DISCUSSION

Splenic flexure is an uncommon site for CRC, and, historically, SFC has been regarded as an entity with poor prognosis. The optimal surgical procedure is still debated (extended vs. limited resections), as demonstrated by two surveys amongst surgeons [25,26] and current literature [27,28]. The laparoscopic approach to the splenic flexure poses different challenges related to its embryology, the relationship with adjacent organs and intrinsic technical steps that are considered demanding even by experienced colorectal surgeons [29]. Furthermore, SFC has been excluded from large randomized controlled trials [11,30,31] assessing the safety and oncological results of laparoscopy for CRC, leading to a lack of standardization for its treatment. Small series from high-volume centres demonstrated that minimally invasive resection of the splenic flexure is feasible [13,15,18,32–34]. However, population-based studies, including our previous publication [1] and two recent large-scale studies by de'Angelis et al. [27] and Degiuli et al. [28] reported that laparoscopy was adopted in just about 60% of SFCs with conversion rates ranging from 6.2% to 9.9%. To the best of our knowledge, this is the largest surgical cohort of SFCs comparing short- and long-term outcomes of laparoscopy versus open surgery after controlling for

TABLE 2 Comparison of surgical procedures and pathological data in the matched population

	LapGroup (n = 130)	OpenGroup (n = 130)	P
Extent of surgery			0.68
Subtotal colectomy	15 (11.5)	11 (8.5)	
Left colonic resection	83 (63.8)	84 (64.6)	
Partial resection	32 (24.6)	35 (26.9)	
Conversion	11 (8.5)	–	–
Anastomosis, stapled	89 (68.5)	67 (51.5)	0.002
Stoma formation	2 (1.5)	4 (3.1)	0.68
Cancer-related resections	7 (5.4)	12 (9.2)	0.34
Specimen characteristics, cm			
Total length, median (IQR)	23 (17.5–34.5)	22 (16–29)	0.44
Proximal margin, median (IQR)	10 (6–15)	10 (7–13.5)	0.82
Distal margin, median (IQR)	8.2 (5.5–13.3)	7.8 (5–11)	0.13
Total no. retrieved LNs, median (IQR)	17.5 (12–25)	15 (11–21)	0.01
No. of cases with <12 LNs	19 (15)	37 (28.9)	0.03

Note:: Values in parentheses are percentages unless differently specified.

Abbreviations: IQR, interquartile range; LN, lymph node.

relevant confounding factors. The significant findings of our study are (i) that laparoscopic surgery is confirmed to be safe and feasible for elective resection of Stages I–III SFC; (ii) compared to open surgery, it is associated with better short-term outcomes; and (iii) that it allows comparable long-term oncological outcomes.

Several single-centre studies based on small numbers of patients showed the feasibility of laparoscopy for SFC [13–22]. Looking at studies comparing laparoscopic and open surgery, Nakashima and colleagues [20] compared 33 patients who underwent laparoscopic surgery for SFC to 22 patients who underwent open surgery, demonstrating improved postoperative outcomes in the LapGroup. Following this publication, Okuda and colleagues [22] retrospectively compared 61 laparoscopic surgeries for SFC with 34 conventional open surgeries, and they demonstrated better recovery outcomes in the laparoscopic group and a similar prognosis. Similarly, Kim and colleagues [19] analysed 18 open and 33 laparoscopic surgeries for SFC concluding that laparoscopy allows better short-term outcomes with comparable long-term results. Nevertheless, none of these papers considered possible biases influencing the allocation of patients to laparoscopic or open surgery, which could, in turn, affect outcomes. More recently, Chi and colleagues [35] compared open and laparoscopic colectomy for SFC after matching through PSM. They retrospectively analysed 62 patients submitted to laparoscopy and 62 patients to open surgery and found no differences in short-term

TABLE 3 Comparison of short-term outcomes in the matched population

	LapGroup (n = 130)	OpenGroup (n = 130)	P
Hospital stay, days, median (IQR)	7 (5–10)	9 (7–15)	0.001
Postoperative 30-day complications	23 (17.7)	43 (33.1)	0.02
Low grade	14 (10.8)	36 (27.7)	0.03
High grade	9 (6.9)	7 (5.4)	0.75
Medical complications	7 (5.4)	15 (11.5)	0.12
Surgical complications	19 (14.6)	32 (24.6)	0.05
Anastomotic leak	2 (1.5)	3 (2.3)	1
Postoperative prolonged ileus	5 (3.8)	13 (10)	0.08
Surgical site infection	2 (1.5)	8 (6.2)	0.10
Redo surgery	6 (4.6)	6 (4.6)	1
30-day unplanned readmission	3 (2.3)	3 (2.3)	1
30-day postoperative mortality	1 (0.8)	2 (1.5)	1
Adjuvant chemotherapy	26 (22.2)	24 (20.5)	0.87
Missing	13 (10)	13 (10)	

Note:: Values in parentheses are percentages unless differently specified.

Abbreviation: IQR, interquartile range.

outcomes and long-term prognosis. Finally, Beghdadi et al. [36] evaluated the results of laparoscopic surgery for SFC in a multicentric European setting. Although the study population was quite large (399 patients with SFC), after application of PSM only 64 patients treated by laparotomy and 64 with laparoscopy were analysed. They also reported improved postoperative outcomes in the laparoscopic group and no differences in terms of OS and disease-free survival.

In our study, a clear benefit in terms of postoperative complications was observed after laparoscopic surgery (17.7% vs. 33.1%; $P = 0.02$). This difference was mostly related to the decrease in surgical complications (14.6% vs. 24.6%; $P = 0.05$) and mild complications (10.8% vs. 27.7%; $P = 0.03$). The improvement in short-term outcomes is reflected by the decrease in LOS, which was 2 days shorter in the LapGroup (7 days [IQR 5–10] vs. 9 days [IQR 7–15]; $P = 0.001$). The results follow the known advantages of laparoscopy for other colon cancer locations in terms of early bowel function restoration and faster recovery [12,20,37].

Although the laparoscopic approach to the splenic flexure is technically challenging, our results confirmed the data published in previous reports [19,34,38] with a conversion rate of 8.5%, almost comparable to other colon cancer locations in experienced hands [38].

Furthermore, our paper demonstrated that laparoscopy did not interfere with the quality of surgical resection. No differences were found for specimen length and resection margins. Moreover, the median number of retrieved nodes was higher in the LapGroup (17.5 [IQR

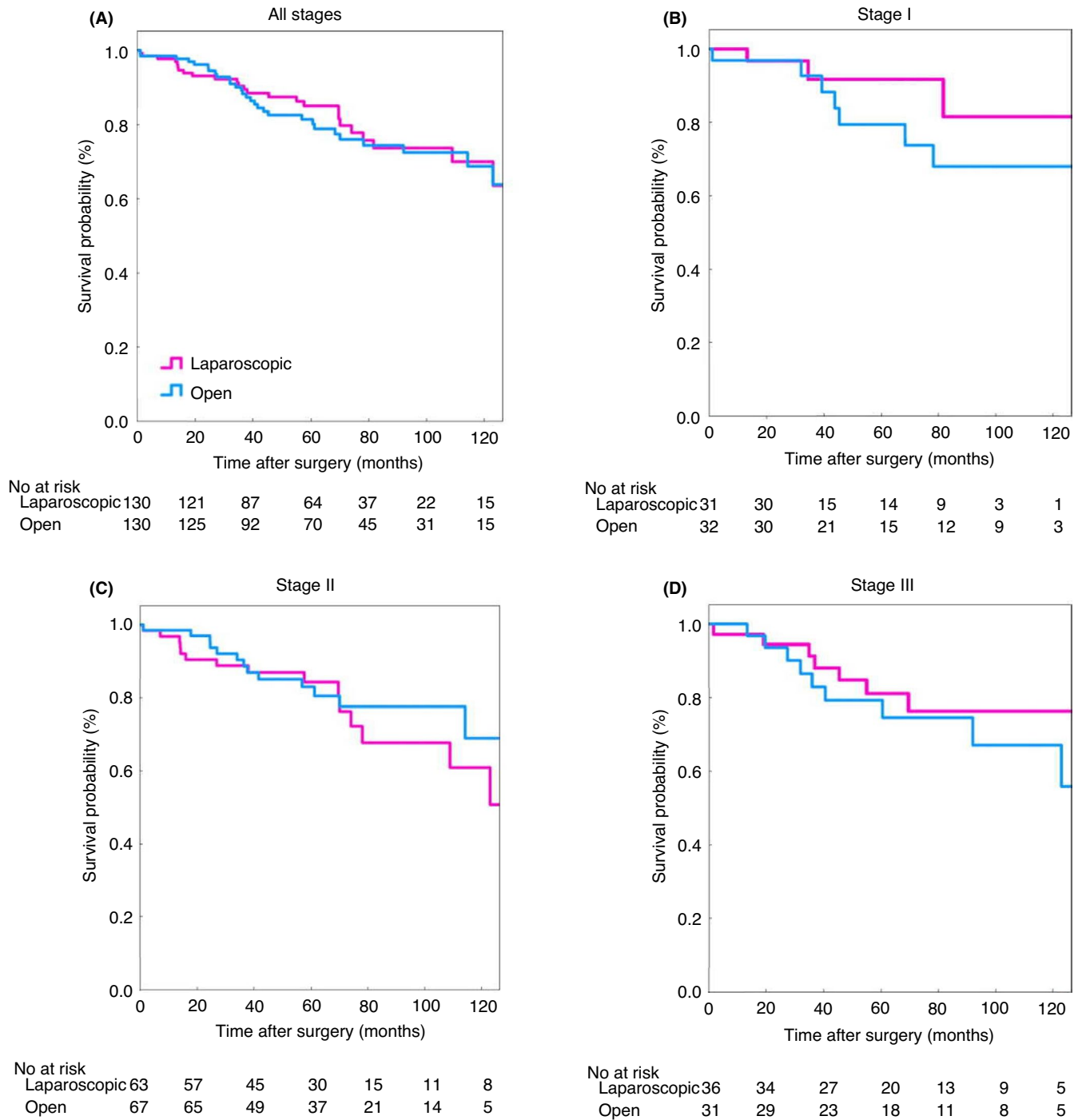


FIGURE 2 Kaplan–Meier estimates of overall survival probability for patients undergoing laparoscopic and open resection for SFC. (A) OS in the whole population ($P = 0.79$); (B) Stage I ($P = 0.26$); (C) Stage II ($P = 0.43$); (D) Stage III ($P = 0.44$)

12–25] vs. 15 [IQR 11–21]; $P = 0.01$) as well as the percentage of patients with more than 12 retrieved nodes (85% vs. 71.1%; $P = 0.03$). This result is in line with previous reports, which associated minimally invasive surgery with a more extensive lymphadenectomy [13,20].

Looking at long-term outcomes, 5-year OS was similar to previous reports [16,17,19,21,22]. Previous studies on SFC [19,33] described similar rates in Stage I–III tumours. Although 5-year OS was slightly better in the LapGroup (85% vs. 81.4%), the difference was

not statistically significant ($P = 0.79$). Similarly, CSS was comparable between open and laparoscopic groups ($P = 0.63$). These results were confirmed even when considering Stages I, II and III separately, as well as at multivariate analysis ($P = 0.72$).

The present study has some limitations, mainly related to its retrospective nature. First, due to the length of the inclusion period, a higher proportion of older cases underwent open surgery. However, this critical issue has been addressed through inclusion

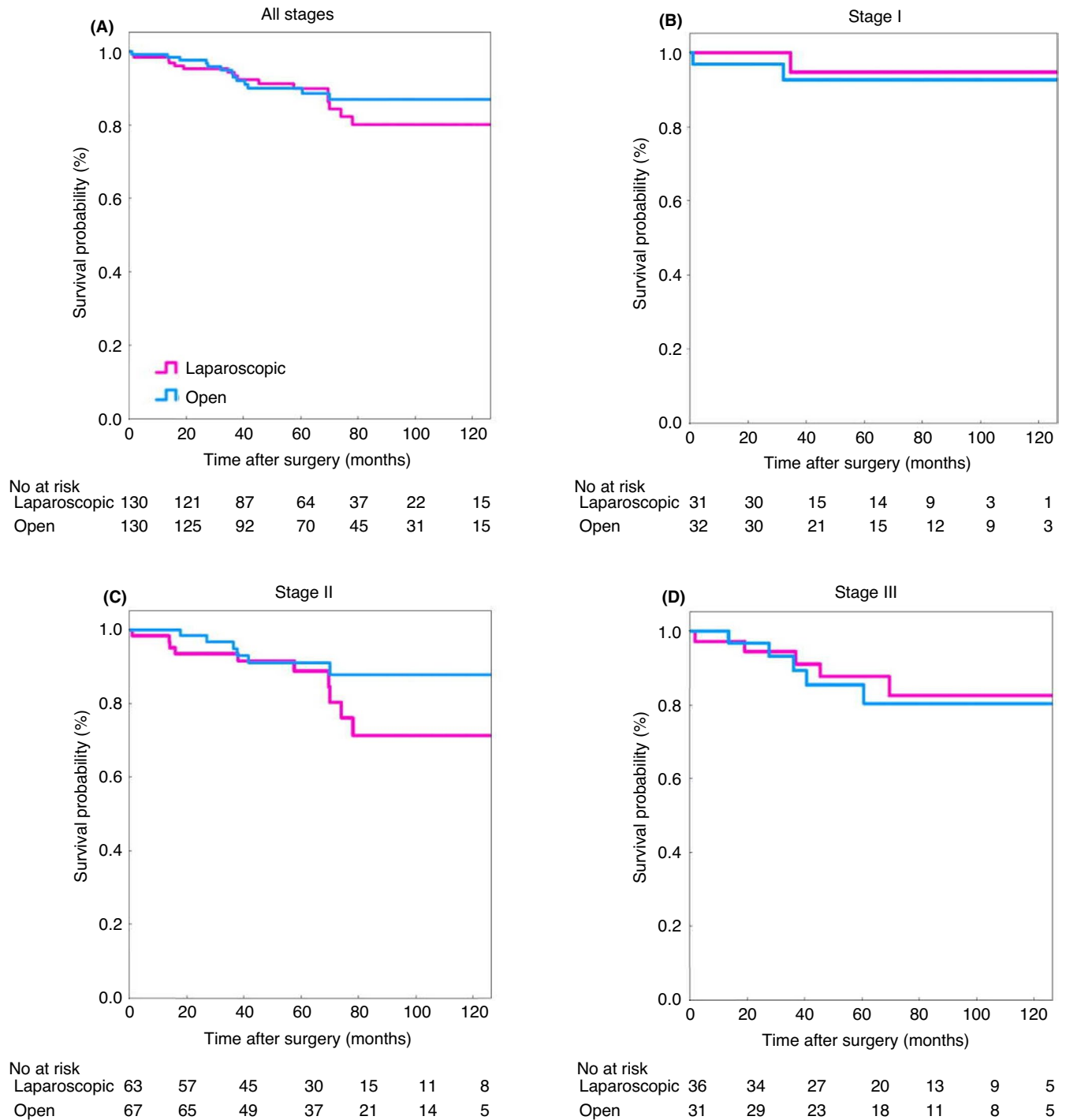


FIGURE 3 Kaplan-Meier estimates of cancer-specific survival probability for patients undergoing laparoscopic and open resection for SFC. (A) CSS in the whole population ($P = 0.63$); (B) Stage I ($P = 0.45$); (C) Stage II ($P = 0.19$); (D) Stage III ($P = 0.77$)

of the period of surgery in the computation of the propensity score. Consequently, the length of follow-up was similar in the laparoscopic and open group, with a median of 5 years. Second, it was not possible to retrieve accurate data on the extent of lymphadenectomy and lymph node involvement level. This drawback was acknowledged and, consequently, the extent of surgery was included among PSM variables. Third, lack of information on intra-operative

data, such as operation time and blood loss, and postoperative recovery items did not permit any inference on these outcomes.

Conversely, our study has the strength to analyse a large and homogeneous cohort of patients with SFC undergoing elective surgery. The application of strict inclusion criteria and the adoption of PSM allowed us to obtain two comparable groups that represent the largest cohort in the current literature.

TABLE 4 Multivariate analysis for OS and CSS performed using the Cox regression model

	OS		CSS	
	HR (95% CI)	P	HR (95% CI)	P
Surgical approach		0.96		0.72
Open	1.0 (reference)		1.0 (reference)	
Laparoscopy	0.9 (0.6–1.7)		1.1 (0.5–2.5)	
Age		<0.001		0.48
≤70	1.0 (reference)		1.0 (reference)	
>70	2.3 (1.2–4.3)		1.3 (0.6–2.9)	
Gender		0.02		0.09
Female	1.0 (reference)		1.0 (reference)	
Male	2 (1.1–3.3)		2 (0.8–5)	
Extent of surgery		0.44		0.78
Left colonic resection	1.0 (reference)		1.0 (reference)	
Subtotal colectomy	0.5 (0.2–1.4)		0.8 (0.2–2.6)	
Partial resection	0.9 (0.5–1.8)		1.2 (0.5–2.8)	
Grading		0.04		0.07
G1–2	1.0 (reference)		1.0 (reference)	
G3	2.0 (1.1–3.8)		2.2 (0.9–5.2)	
TNM stage		0.05		0.03
Stage I	1.0 (reference)		1.0 (reference)	
Stage II	1.4 (1.1–2.9)		1.6 (1.1–5.2)	
Stage III	2.4 (1.2–6.2)		2.4 (1.4–9.7)	
Adjuvant chemotherapy		0.16		0.99
No	1.0 (reference)		1.0 (reference)	
Yes	0.6 (0.3–1.3)		1.0 (0.4–2.9)	

Abbreviations: CSS, cancer-specific survival; HR, hazard ratio; OS, overall survival.

CONCLUSION

Laparoscopy is safe and effective for the curative treatment of Stages I–III SFC. It is associated with better short-term results with reduced complication rates and postoperative LOS. Moreover, laparoscopic surgery appears to provide excellent long-term cancer outcomes.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Corrado Pedrazzani <https://orcid.org/0000-0003-2431-6117>

Giulia Turri <https://orcid.org/0000-0001-6150-6812>

Soo Yeun Park <https://orcid.org/0000-0003-4821-2101>

Koya Hida <https://orcid.org/0000-0001-7210-7075>

Yudai Fukui <https://orcid.org/0000-0002-7262-7975>

Jacopo Crippa <https://orcid.org/0000-0003-4090-0989>

Giovanni Ferrari <https://orcid.org/0000-0002-5405-9046>

Matteo Origi <https://orcid.org/0000-0003-4191-3378>

Gaya Spolverato <https://orcid.org/0000-0002-7275-2573>

Matteo Zuin <https://orcid.org/0000-0002-3571-0120>

Sung Uk Bae <https://orcid.org/0000-0002-7876-4196>

Seong Kyu Baek <https://orcid.org/0000-0001-6427-8675>

Gyung Mo Son <https://orcid.org/0000-0002-8861-6293>

Timothy Rockall <https://orcid.org/0000-0001-8488-7005>

Alfredo Guglielmi <https://orcid.org/0000-0003-1713-4307>

Gyu Seog Choi <https://orcid.org/0000-0001-5476-4610>

REFERENCES

- Pedrazzani C, Turri G, Park SY, Hida K, Fukui Y, Crippa J, et al. Clinical-pathologic characteristics and long-term outcomes of left flexure colonic cancer: a retrospective analysis of an international multicenter cohort. *Dis Colon Rectum*. 2020;63(12):1593–601.
- Steffen C, Bokey EL, Chapuis PH. Carcinoma of the splenic flexure. *Dis Colon Rectum*. 1987;30(11):872–4. [cited 2019 Jun 23] Available from: <http://www.ncbi.nlm.nih.gov/pubmed/3677963>
- Aldridge MC, Phillips RKS, Hittinger R, Fry JS, Fielding LP. Influence of tumour site on presentation, management and subsequent outcome in large bowel cancer. *Br J Surg*. 2005;73(8):663–70. [cited 2019 Jun 23]. <https://doi.org/10.1002/bjs.1800730829>
- Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H. Comparison of 17,641 patients with right- and left-sided colon

- cancer: differences in epidemiology, perioperative course, histology, and survival. *Dis Colon Rectum*. 2010;53(1):57–64.
5. Kim CW, Shin US, Yu CS, Kim JC. Clinicopathologic characteristics, surgical treatment and outcomes for splenic flexure colon cancer. *Cancer Res Treat*. 2010;42(2):69–76.
 6. Nakagoe T, Sawai T, Tsuji T, Jibiki M, Nanashima A. Carcinoma of the splenic flexure: multivariate analysis of predictive factors for clinicopathological characteristics and outcomes after surgery. *J Gastroenterol*. 2000;35:528–35.
 7. Levien DH, Gibbons S, Begos D, Byrne DW. Survival after resection of carcinoma of the splenic flexure. *Dis Colon Rectum*. 1991;34(5):401–3 [cited 2019 Jun 23]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/2022146>
 8. Benedix F, Schmidt U, Mroczkowski P, Gastinger I, Lippert H, Kube R, et al. Colon carcinoma—classification into right and left sided cancer or according to colonic subsite?—analysis of 29 568 patients. *Eur J Surg Oncol*. 2011;37(2):134–9. <https://doi.org/10.1016/j.ejso.2010.12.004>
 9. Martel G, Crawford A, Barkun JS, Boushey RP, Ramsay CR, Fergusson DA. Expert opinion on laparoscopic surgery for colorectal cancer parallels evidence from a cumulative meta-analysis of randomized controlled trials. *PLoS One*. 2012;7(4):e35292.
 10. Kuhry E, Schwenk WF, Gaupset R, Romild U, Bonjer HJ. Long-term results of laparoscopic colorectal cancer resection. *Cochrane Database Syst Rev*. 2008;2008(2):CD003432. <https://doi.org/10.1002/14651858.CD003432.pub2>
 11. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet*. 2005;365(9472):1718–26. [cited 2019 Jul 31]. Available from: <https://www.sciencedirect.com/science/article/pii/S0140673605665452?via%3Dihub>
 12. Veldkamp R, Kuhry E, Hop WCJ, Jeekel J, Bonjer HJ, Haglind E. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol*. 2005;6(7):477–84.
 13. Grieco M, Cassini D, Spoletoni D, Soligo E, Grattarola E, Baldazzi G, et al. Laparoscopic resection of splenic flexure colon cancers: a retrospective multi-center study with 117 cases. *Updates Surg*. 2019;71(2):349–57. <https://doi.org/10.1007/s13304-018-0601-x>
 14. Ceccarelli G, Biancafarina A, Patrì A, Spaziani A, Bartoli A, Bellochi R, et al. Laparoscopic resection with intracorporeal anastomosis for colon carcinoma located in the splenic flexure. *Surg Endosc*. 2010;24(7):1784–8. [cited 2019 Jun 26]. Available from: <https://link.springer.com/content/pdf/10.1007%2Fs00464-009-0853-0.pdf>
 15. Ceretti AP, Maroni N, Sacchi M, Bona S, Angiolini MR, Bianchi P, et al. Laparoscopic colonic resection for splenic flexure cancer: our experience. *BMC Gastroenterol*. 2015;15(76):1–6. <https://doi.org/10.1186/s12876-015-0301-7>
 16. de'Angelis AN, Hain E, Disabato M, Cordun C, Carra MC, Azoulay D, et al. Laparoscopic extended right colectomy versus laparoscopic left colectomy for carcinoma of the splenic flexure: a matched case–control study. *Int J Colorectal Dis*. 2016;31:623–30.
 17. Gravante G, Elshaer M, Parker R, Mogeckwu AC, Drake B, Aboelkassem A, et al. Extended right hemicolectomy and left hemicolectomy for colorectal cancers between the distal transverse and proximal descending colon. *Ann R Coll Surg Engl*. 2016;98(5):303–7.
 18. Han K-S, Choi G-S, Park J-S, Kim HJ, Park SY, Jun S-H. Short-term outcomes of a laparoscopic left hemicolectomy for descending colon cancer: retrospective comparison with an open left hemicolectomy. *J Korean Soc Coloproctol*. 2010;26(5):347. [cited 2019 Jun 26]. Available from: www.coloproctol.org
 19. Kim MK, Lee IK, Kang WK, Cho HM, Kye BH, Jalloun HE, et al. Long-term oncologic outcomes of laparoscopic surgery for splenic flexure colon cancer are comparable to conventional open surgery. *Ann Surg Treat Res*. 2017;93(1):35–42. [cited 2021 Jan 20]. Available from: <https://pubmed.ncbi.nlm.nih.gov/35507789/>
 20. Nakashima M, Akiyoshi T, Ueno M, Fukunaga Y, Nagayama S, Fujimoto Y, et al. Colon cancer in the splenic flexure: comparison of short-term outcomes of laparoscopic and open colectomy. *Surg Laparosc Endosc Percutan Tech*. 2011;21(6):415–8. [cited 2019 Jun 26] Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22146163>
 21. Odermatt M, Siddiqi N, Johns R, Miskovic D, Khan O, Khan J, et al. The short-and long-term outcomes for patients with splenic flexure tumours treated by left versus extended right colectomy are comparable: a retrospective analysis. *Surg Today*. 2014;44(11):2045–51. [cited 2019 Jun 26]. Available from: <https://link.springer.com/content/pdf/10.1007%2Fs00595-013-0803-2.pdf>
 22. Okuda J, Yamamoto M, Tanaka K, Masubuchi S, Uchiyama K. Laparoscopic resection of transverse colon cancer at splenic flexure: technical aspects and results. *Updates Surg*. 2016;68(1):71–5. [cited 2021 Feb 22] <https://doi.org/10.1007/s13304-016-0352-5>
 23. 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.
 24. Mike M, Kano N. Reappraisal of the vascular anatomy of the colon and consequences for the definition of surgical resection. *Dig Surg*. 2013;30:383–92.
 25. Manceau G, Benoist S, Panis Y, Rault A, Mathonnet M, Goere D, et al. Elective surgery for tumours of the splenic flexure: a French inter-group (AFC, SFC, FRENCH, GRECCAR) survey. *Tech Coloproctol*. 2020;24(2):191–8. <https://doi.org/10.1007/s10151-019-02143-2>
 26. Chan D, Shah P, Soanes M, Saklani A. Current trends and controversies in the management of patients with splenic flexure tumours. *J Cancer Res Ther*. 2013;1(1):8–10.
 27. de'Angelis N, Martínez-Pérez A, Winter DC, Landi F, Vitali GC, Le Roy B, et al. Extended right colectomy, left colectomy, or segmental left colectomy for splenic flexure carcinomas: a European multicenter propensity score matching analysis on behalf of the SFC Study Group. *Surg Endosc*. 2021;35(2):661–72. [cited 2020 Feb 22] <https://doi.org/10.1007/s00464-020-07431-9>
 28. Degiuli M, Reddavid R, Ricceri F, Di Candido F, Ortenzi M, Elmore U, et al. Segmental colonic resection is a safe and effective treatment option for colon cancer of the splenic flexure: a nationwide retrospective study of the Italian Society of Surgical Oncology—Colorectal Cancer Network Collaborative Group. *Dis Colon Rectum*. 2020;63(10):1372–82. <https://doi.org/10.1097/DCR.0000000000001743>
 29. Jamali FR, Soweid AM, Dimassi H, Bailey C, Leroy J, Marescaux J, et al. Evaluating the degree of difficulty of laparoscopic colorectal surgery. *Arch Surg*. 2008;143(8):762. <https://doi.org/10.1001/archsurg.143.8.762>
 30. van der Pas MHGM, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WCJ, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol*. 2013;14(3):210–8. [cited 2019 May 11] Available from: <http://www.color2.org/>
 31. Green BL, Marshall HC, Collinson F, Quirke P, Guillou P, Jayne DG, et al. Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. *Br J Surg*. 2013;100:75–82. <https://doi.org/10.1002/bjs.8945>
 32. Carlini M, Spoletoni D, Castaldi F, Giovannini C, Passaro U. Laparoscopic resection of splenic flexure tumors. *Updates Surg*. 2016;68(1):77–83. <https://doi.org/10.1007/s13304-016-0357-0>



33. Yamaguchi S, Tashiro JO, Araki R, Okuda J, Hanai T, Otsuka K, et al. Laparoscopic versus open resection for transverse and descending colon cancer: short-term and long-term outcomes of a multicenter retrospective study of 1830 patients. *Asian J Endosc Surg*. 2017;10(3):268–75. <https://doi.org/10.1111/ases.12373>
34. Ardu M, Bergamini C, Martellucci J, Prosperi P, Valeri A. Colonic splenic flexure carcinoma: is laparoscopic segmental resection a safe enough oncological approach? *Surg Endosc*. 2020;34(10):4436–43. <https://doi.org/10.1007/s00464-019-07221-y>
35. Chi Z, Li Z, Cheng L, Wang C. Comparison of long-term outcomes after laparoscopic-assisted and open colectomy for splenic flexure cancer. *J BUON*. 2018;23(2):322–8.
36. Beghdadi N, Martínez-Pérez A, Winter DC, Landi F, Vitali GC, Le Roy B, et al. European multicenter propensity score match study of laparoscopic vs. open colectomy for splenic flexure carcinomas: results from the Splenic Flexure Cancer (SFC) Study Group. *J Visc Surg*. 2021. [cited 2021 Jul 16] Available from: <https://doi.org/10.1016/j.jviscsurg.2021.06.007>
37. Martínez-Pérez A, Brunetti F, Vitali GC, Abdalla S, Ris F, de'Angelis N. Surgical treatment of colon cancer of the splenic flexure: a systematic review and meta-analysis. *Surg Laparosc Endosc Percutan Tech*. 2017;27(5):318–27. [cited 2019 Feb 10] Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28796653>
38. Bracale U, Merola G, Pignata G, Corcione F, Pirozzi F, Cuccurullo D, et al. Laparoscopic resection with complete mesocolic excision for splenic flexure cancer: long-term follow-up data from a multicenter retrospective study. *Surg Endosc*. 2020;34(7):2954–62. [cited 2019 Nov 23] <https://doi.org/10.1007/s00464-019-07078-1>

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Pedrazzani C, Turri G, Park SY, Hida K, Fukui Y, Crippa J, et al. Laparoscopic versus open surgery for left flexure colon cancer: a propensity score matched analysis from an international cohort. *Colorectal Dis*. 2021;00:1–11. <https://doi.org/10.1111/codi.15962>