Clinics in Surgery

Research Article
Published: 03 Mar, 2021

Splenic Flexure Cancer: Segmental Colonic Resection, Left Hemicolectomy, Extended Right Hemicolectomy or Total Colectomy? Short-Term and Long-Term Outcomes

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Abstract

Introduction: Splenic flexure tumors are quite rare, accounting for 2% to 8% of all colorectal cancers. The heterogeneity of the vascular support and lymphatic drainage of the splenic flexure make the surgical management complex and non-standardized. The aim of the study is to compare the four surgical techniques (extended right hemicolectomy, left hemicolectomy, segmental colonic resection, and total colectomy) in terms of short-term and long-term outcomes.

Materials and Methods: Consecutive patients from two hospitals of Turin (the Martini hospital and the San Giovanni Bosco hospital) between September 1998 and March 2020 have surgical visit for splenic flexure cancer. The data reported in the database include preoperative, postoperative, histopathological characteristics, and survival results. Univariate and multivariate analysis are performed to evaluate the confounding factors influencing overall and disease-free survival.

Results and Discussion: A total of 173 patients treated for splenic flexure tumors are included in the study. The four groups are similar on the baseline characteristics of the patients. Clavien Dindo ≥ 3 postoperative complications and 30-day mortality are comparable in the four groups (p=0.216 e p=0.213). Five-year overall survival and progression-free survival did not show significant differences between the four surgical techniques (p=1.08 e p=0.28). No statistically significant differences were found between the four groups for baseline patient characteristics, intraoperative outcomes, postoperative complications, and TNM staging.

Conclusion: Segmental colonic resection, extended right hemicolectomy, left hemicolectomy and total colectomy show no significant difference in short-term and oncological outcomes in cancer of the splenic flexure. Further studies with a higher level of evidence are needed.

Keywords: Cancer of the splenic flexure; Left hemicolectomy; Extended right colectomy; Limited resection; Resection of the splenic flexure; Segmental colonic resection

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Received Date: *18 Jan 2021*

Accepted Date: *19 Feb 2021*

Published Date: *03 Mar 2021*

Citation:

Bono D, Galati S, Potenza E, Loddo F, Bonaccors L, Viora T, et al. Splenic Flexure Cancer: Segmental Colonic Resection, Left Hemicolectomy, Extended Right Hemicolectomy or Total Colectomy? Short-Term and Long-Term Outcomes. Clin Surg. 2021; 6: 3089.

Introduction

Colorectal cancer is the second most common cancer-related cause of death in men and the third most common in women in Europe [1]. Splenic flexure cancer is defined as colonic cancer located in the distal third of the transverse colon, in the left colonic angle, or in the proximal descending colon within 10 cm from the left colonic flexure [2].

It is quite rare, accounting for 2% to 8% of all colorectal cancers; it tends to occur at a more advanced stage and is associated with a higher rate of intestinal obstruction [3,4].

The anatomical heterogeneity of the vascular support and lymphatic drainage of the splenic flexure of the colon make the surgical management of tumors of this site complex [5]. Consequently, the optimal surgical strategy is not standardized [6,7].

Cancers of the splenic flexure can be approached with three different surgical techniques: Extended right hemicolectomy, left hemicolectomy, and segmental colonic resection.

The first involves resection of the terminal ileum, right and transverse colon up to the middle descendent, with ligation of the ileocolic, right, middle, and left colic arteries [8].

Left hemicolectomy involves a high ligation of the inferior mesenteric artery and the left branch of the middle colic artery, followed by a transverse-rectal anastomosis, or a selective ligation of the left colic artery with transverse-sigmoid anastomosis [4-9]. Finally, segmental colonic resection involves the ligation of the left colic artery and the left branch of the middle colic artery with the creation of a colocolic anastomosis after resection of the distal tract of the transverse colon, the splenic flexure, and the proximal descending colon. In addition to the three techniques mentioned above, cancers of the splenic flexure can be treated with a fourth surgical technique, total or subtotal colectomy especially in an emergency setting with intestinal obstruction.

However, there is no general and unanimous consensus on the extent of surgical resection in tumors of the splenic flexure [10]. In fact, the current literature does not show significant differences between extended right hemicolectomy, segmental colonic resection, and left hemicolectomy on short-term and long-term outcomes [11-13].

The aim of our study is to compare the four surgical techniques of treatment of splenic flexure cancer, namely left hemicolectomy, extended right hemicolectomy, segmental colonic resection and total colectomy in terms of short and long-term results.

Materials and Methods

This study is a retrospective analysis of a prospective multi-center database. Consecutive patients received a surgical visit at two hospitals in Turin (Martini Hospital and San Giovanni Bosco Hospital) between September 1998 and March 2020 for endoscopic finding of lesions located 10 cm above and below the left colic angle with biopsy of adenocarcinoma or endoscopically non-removable adenomas.

The data reported in the database include: the preoperative characteristics of the patients, the intraoperative ones, the short-term postoperative ones, the histopathological ones, and the oncological survival data.

Preoperative characteristics are as follows: age, gender, diabetes, heart disease, lung disease, liver disease, American Society of Anesthesiologists' (ASA) score, patient comorbidities assessed with the Charlson Comorbidity Index (CCI) and use of anticoagulants or antiplatelet agents [14,15].

Operative and postoperative features include: Operative time, laparoscopic or laparotomic approach, other associated resections, elective or urgent regimen, types of anastomosis, mean hospital stay, complication rate according to the Clavien-Dindo score [16]. In particular, the rates of anastomotic dehiscence, surgical wound infection rate, and intestinal occlusion rate, cardiac and respiratory complications were recorded.

The histopathological characteristics are: The histotype (adenocarcinoma, adenoma, or others), T (T1, T2, T3, T4), N (N1, N2, N3, N4), M (according to the 8th pTNM staging system [17]), degree of differentiation, number of lymph nodes harvested, state of margins.

Preoperative mechanical bowel preparation in patients in elective surgery of both hospitals (polyethylene glycol solution 4 L 48 h before surgery) was administered to all patients until December 2010; therefore, according to the results of the meta-analysis published by Slim et al. [18]. It was abandoned, and all patients had a slag-free diet for five preoperative days and rectal enema the night before surgery.

Perioperative management in both hospitals was uniform. Intravenous antibiotics (cephalosporin or gentamicin in case of known allergy to cephalosporin and metronidazole) were administered before starting the surgery and in the first 24 h. The subcutaneous injection of low molecular weight heparin and elastic stockings were used to obtain the prophylaxis of deep vein thrombosis. The postoperative management of the patient (analgesia, prophylaxis of nausea and vomiting, removal of the urinary catheter, patient mobilization, and oral intake) was also uniform in the two hospitals. The patient is discharged after recovering mobilization and bowel function, in the absence of complications, with pain successfully controlled by oral medications and adequate oral food intake.

The operations were performed by surgeons with extensive experience in open colorectal and advanced laparoscopic surgery.

Follow-up was standardized based on the guidelines of the Italian Association of Medical Oncology [19].

Statistical analysis

Quantitative data are provided as mean and standard deviation, while categorical data are expressed as percentages. The statistical analysis between the groups was performed using the chi square test or the Wilconxon test with α=0.05.

For the analysis of comorbidities in colorectal surgery it was decided to use a cut off CCI<3 (low rate of comorbidity) and CCI ≥ 3 (high rate of comorbidity).

With the use of the Kaplan-Meier estimates, we want to evaluate the Overall Survival (OS), and the Progression-Free Survival (PFS) between the four groups. Furthermore, we have calculated with Kaplan Meier curves the overall survival of colonic segmental resection with the cumulative one of extended resections (left hemicolectomy and extended right hemicolectomy) in accordance with the study by De Giuli et al. [20] Statistical significance was assessed with the log rank test (with α=0.05).

A univariate and multivariate analysis was performed to evaluate the confounding factors affecting OS and PFS between the four groups with the Cox regression model. The following variables were considered: type of surgery, ASA score, CCI score, staging, number of lymph nodes harvested, elective or urgency setting, anastomotic dehiscence rate, surgical wound infection rate, rate of hemorrhage, of intestinal perforation, of intestinal obstruction, Clavien-Dindo score and rate of medical and surgical complications. Results are reported as odds ratios (ORs) with 95% Confidence Intervals (CI). The statistical analysis is performed using Stat plus Pro (Copyright© 2021 AnalystSoft Inc.).

Surgical techniques

To assess the quality of surgery, all operative reports were reviewed at each participating center and proper ligation of the LCA (Left Colic Artery), left or main branch of the MCA (Middle Colic Artery), IMA (Inferior Mesenteric Artery), and ileocolic artery, and/or approximate peripheral ligations assessed.

Left hemicolectomy: open and laparoscopic

At both hospitals, laparotomic left hemicolectomy is performed with a xiphopubic incision. Then, we make exploration of the abdominal cavity with palpation of the primary lesion, search for

synchronous colic lesions, liver metastases and peritoneal carcinosis. We continue with dissection of the left paracolic gutter in the avascular plane between Told's and Gerota's fascia. Identification of the left ureter. Coloepiploic detachment and lowering of the splenic flexure are completed. Isolation, ligation, and section of the IMA at the aortic origin (with or without preservation of the LCA) and of the Inferior Mesenteric Vein (IMV) at the duodenal-jejunal junction are achieved.

The rectal section is then performed at the rectosigmoid joint. We have a colonic section at the mediodistal transverse about 5 cm proximal to the hetero plastic lesion with linear mechanical staplers.

Regarding the restoration of intestinal continuity, at both hospitals, from 1998 to 2014 a manual colo-colonic anastomosis with detached points of Vicryl 3/0 (posterior and anterior wall) was performed mainly.

From 2014 to 2020, at the Martini Hospital, the second prevalent anastomosis technique was laterolateral colocolic anastomosis with circular mechanical suture type EA 26 or 29 mm. The head of the circular suturing machine was fixed in the proximal colic segment with a tobacco bag in 2/0 prolene or with pursestring, subsequent colotomy on the distal colic segment with the anvil coming out of the distal colic linear suture.

The third type prevalent at the Martini Hospital and San Giovanni Bosco is the mechanical terminoterminal colocolic anastomosis according to Knight-Griffen's.

At the San Giovanni Bosco hospital, the second prevalent type is the manual isoperistaltic colocolic anastomosis in double layer (anterior and posterior intestinal wall).

In laparoscopy, in both hospitals, left hemicolectomy begins with the induction of pneumoperitoneum at 12 mmHg with Hasson's trocar in the supraumbilical area. Then, we carry on the placement of other three trocar (12 mm in the right iliac region, 5 mm in the left iliac region and 5mm in hypogastrium). We proceed with the isolation and section of the IMV and opening of the plane between Told's and Gerota's fascia up to the IMA which is sectioned between clips. We then continue with the section of the left gastrocolic and splenocolic ligament with lowering of the splenic flexure. We obtain the liberation of the left paracolic gutter. Finally, we achieve the rectal section at the level of the rectosigmoid joint with a laparoscopic linear stapler.

The suprapubic service incision is performed with externalization of the operative piece, colonic section at the level of the middle transverse colon and positioning of the head of the mechanical circular stapler. A colocolic terminoterminal anastomosis is performed according to Knight-Griffen's.

At the San Giovanni Bosco hospital, a double layer manual extracorporeal colocolic anastomosis was performed until 2006.

Segmental colonic resection: open and laparoscopic

Laparotomic Segmental Colonic Resection is performed, in both hospital centers, with supra-sub-umbilical incision and exploration of the abdominal cavity. The isolation of the middle distal transverse colon continues with coloepiploic detachment and mobilizations of the splenic flexure are done. Then, we continue with dissection of the proximal and middle descending colon. Isolation, ligation, and section of the left colic vessels at the origins of IMA are made in accordance with the study of Reddavid et al. [21]. Finally, the colic section proximal to the mid-distal transverse and the colic section distal to the medial descendent were performed with linear mechanical sutures. The colocolic anastomosis techniques after segmental resection are the same as those used in left hemicolectomy.

In Laparoscopy, pneumoperitoneum with supraumbilical Hasson's trocar is performed and three other operative trocars are placed (5 mm in left iliac region and left hypochondrium and 10 mm in right iliac region). Afterwards, we have the section of the gastrocolic ligament with lowering of the splenic flexure. We proceed with the incision of the posterior peritoneum with isolation of the IMA and section of the LCA at the origin. Isolation and section of the IMV emerging from the pancreas are done. Finally, we performed the medium lateral detachment between Told's and Gerota's fascia, mobilization of the sigma. Preparation of the proximal third of the transverse colon and the colo-sigmoid passage.

At the San Giovanni Bosco hospital, a transverse descending laterolateral extracorporeal isoperistaltic anastomosis or an extracorporeal manual terminal is performed.

Extended right hemicolectomy: open and laparoscopic

At both hospitals, laparotomic extended right hemicolectomy is performed with a right supra-sub-umbilical or transverse incision and subsequent exploration of the abdominal cavity. Then, we continue with dissection of the right paracolic gutter on the avascular plane between the fascia of Told and Gerota. We have identified the right ureter. We have completed the lowering of the hepatic flexure and section of the right gastrocolic ligament. We proceed with the isolation of the last ileal loop up to about 10 cm from the ileocecal valve. Isolation of the transverse colon and the splenic flexure are completed.

Isolation, ligation, and section of the ileocolic vessels at the origin of the superior mesenteric vessels are done. Then, we performed ligation and section of the right colic branches of the middle colic vessels. The ileal and colic section on the proximal descendent colon followed.

At the Martini Hospital, two anastomotic techniques prevail for ileocolic anastomosis.

In the past, a mechanical terminolateral ileo-descendent anastomosis was performed with a circular mechanical stapler type EA 26 or 29 mm. The head of the circular stapler was fixed in the ileal segment with a tobacco bag in 2/0 prolene or with pursestring, subsequent colotomy on the colonic segment with the anvil coming out of the linear colic suture.

Since 2015, a laterolateral anisoperistaltic mechanical ileocolic anastomosis has also been performed with a linear mechanical stapler. In it, the coloileal stump was closed with the linear mechanical stapler and then we have completed with haemostatic reinforcement suture with Vicryl 2/0.

At the San Giovanni Bosco Hospital, a manual ileo-descendent anastomosis is performed in double layer (posterior and anterior intestinal wall) in Vicryl 3/0.

In laparoscopy, at both centers, extended right hemicolectomy begins with the induction of the pneumoperitoneum at 12 mmHg CO_2 after introducing the umbilical Hasson's trocar. Three additional trocars are placed in the left iliac region (5 mm), left hypochondrium

Table 1: Baseline characteristics of patients.

	Segmental colonic resection (n=57)	Left hemicolectomy (n=57)	Extended right hemicolectomy (n=36)	Total colectomy (n=23)	p value
Age (years), mean, SD	70.10 (12.5)	71.57 (9.8)	73.58 (11.8)	72.54 (9.2)	0.551
Male gender, n (%)	36 (63.1)	38 (66.6)	22 (61.1)	14 (60.8)	0.788
ASA score, n (%)					0.413
1	4 (7)	8 (14)	8 (22.2)	3 (13.6)	
2	43 (75.4)	40 (70.2)	22 (61.1)	13 (59)	
3	10 (17.5)	9 (15.8)	6 (16.7)	6 (16.7)	
4	0	0	0	0	
CCI, mean, SD	3.40 (1.8)	3.50 (1.6)	3.50 (1.5)	3.77 (1.8)	0.87
CCI ≥ 3, n, (%)	34 (62.9)	43 (75.4)	25 (69.4)	17 (73.9)	0.14
Diabetes, n (%)	10 (17.5)	12 (21)	7 (19.4)	2 (9)	0.659
Cardiopathy, n (%)	47 (82.5)	48 (84.2)	27 (75)	20 (90.9)	0.457
Hepatopathy, n (%)	0	3 (5.2)	1 (2.8)	0	0.253
Pneumopathy, n (%)	7 (12.3)	4 (7)	3 (8.3)	4 (17.4)	0.476
Use of anticoagulants n (%)	25 (43.8)	24 (42.1)	18 (50)	11 (47.8)	0.849
San Giovanni Bosco hospital, n (%)	25 (43.8)	38 (66.6)	22 (61.1)	21 (91.3)	0.0003
Martini hospital, n (%)	32 (56.2)	19 (33.4)	14 (38.9)	2 (8.7)	

ASA: American Society of Anesthesiologists; SD: Standard Deviation; CCI: Charlson Comorbidity Index

(10 mm), right lumbar region (5 mm). The right colonic frame is arranged, highlighting the salience of the ileocolic vessels. Then, we continue with dissection along the avascular plane until the plane between Told's and Gerota's fascia is highlighted. Along this plane the dissection is prolonged in the cranial and caudal direction until the cecal pole is mobilized with the last ileal loop and the duodenum is visualized. Isolation and selective section between ileocolic vessel clips are done. We proceed with dissection of the root of the transverse mesocolon until the middle colic vessels are isolated, which are also tied with clips. Then we have also the dissection of the right paracolic gutter up to the hepatic flexure. We have opened the gastrocolic ligament from the midline to the right until it meets the plane of colic mobilization, breaking down the flexure. It continues with the opening of the gastrocolic to the left until below the splenic flexure.

At the San Giovanni Bosco hospital, the service incision is performed and a double-layer extracorporeal laterolateral isoperistaltic ileocolic anastomosis is done.

At the Martini hospital, on the other hand, an extracorporeal mechanical anisoperistaltic laterolateral ileocolic anastomosis is usually performed.

Total colectomy

In both hospitals, laparotomic total colectomy is performed with xiphopubic median laparotomy and exploration of the abdominal cavity. Then, we proceed with the right hemicolectomy with a lateromedial approach. Then, we continue with the dissection of the right paracolic gutter. Detachment and section of the right and left gastrocolic ligaments are done. We have lowered the left and right colonic flexure. Isolation and section of the right colic, ileocolic and middle colic vessels are done. Subsequent, left hemicolectomy with initial dissection of the left paracolic gutter are completed. We proceed with dissection of the descending colon, the sigma, and the proximal rectus. Isolation and section of the inferior mesenteric vessels are done. Then, we continue with section of the proximal rectum with a linear mechanical stapler, isolation and section of the last ileal loop.

At the San Giovanni Bosco Hospital, three main types of anastomosis were performed to restore intestinal continuity: manual isoperistaltic laterolateral ileo-sigmoid, manual terminoterminal ileo-rectal or manual laterоterminal ileo-rectal anastomosis.

Instead, the prevalent type of anastomosis at the Martini hospital is the mechanical laterоterminal ileo-rectal according to Knight-Griffen's.

Results

A total of 173 patients treated with surgery for splenic flexure tumors were included in the study: 57 (33.14%) underwent segmental colonic resection, 57 (33.14%) left hemicolectomy, 36 (20.93%) had extended right hemicolectomy, and 23 (12.79%) total colectomy. Among the patients included, 67 (38.73%) had undergone surgery at the Martini Hospital and 106 (61.23%) at the San Giovanni Bosco Hospital. The baseline characteristics of the patients are reported in Table 1. No significant differences were identified between the four groups in terms of age, sex, ASA score, diabetes, heart disease, liver disease, pulmonary disease and use of anticoagulants. More total colectomy and fewer segmental colonic resections were performed at the San Giovanni Bosco Hospital than at the Martini hospital (p=0.0003).

Intraoperative results

Most patients underwent a laparotomy approach (157 patients). 128 (74.4%) patients are subjected to elective surgery and 44 (25.6%) to urgent surgery. The intraoperative characteristics are described in Table 2. The overall mean operative time is 210 min (SD 65.60).

No significant differences are observed between the four groups on mean operative time, rate of laparoscopy or laparotomy and rate of other resections associated.

There is a significant difference in the rate of elective or emergency surgery due to a prevalence of left hemicolectomy and segmental colonic resection in elective rather than in emergency setting (p=0.0001).

Table 2: Intraoperative results.

	Segmental colonic resection (n=57)	Left hemicolectomy (n=57)	Extended right hemicolectomy (n=36)	Total colectomy (n=23)	p value
Operative time, minutes	196.92 (59.7)	215.08 (71.5)	211.11(73)	235 (35.6)	0.06
Laparoscopy, n (%)	4(7)	8 (14)	3 (8.3)	0	0.228
Laparotomy, n (%)	53 (93)	49 (86)	33 (91.7)	22 (100)	0.227
Elective surgery, n (%)	53 (92.8)	46 (80.7)	18 (50)	11 (47.8)	0.0001
Other resections associated, n (%)	8 (14)	12(21)	7 (19.4)	1 (4.5)	0.301

Table 3: Postoperative results.

	Segmental colonic resection (n=57)	Left hemicolectomy (n=57)	Extended right hemicolectomy (n=36)	Total colectomy (n=23)	Total (n=173) (%)	p value
Global complications, n (%)	14 (24.6)	16 (28)	6 (16.7)	5 (22.7)	41 (23.7)	0.656
Clavien -Dindo ≥ 3 n (%)	6 (10.5)	8 (14)	5 (13.9)	2 (9)	21 (12.1)	0.216
Anastomotic dehiscence, n (%)	4 (7)	4 (7)	5 (13.9)	0	13 (7.5)	0.271
Intestinal obstruction, n (%)	1 (1.8)	0	0	0	1 (0.6)	0.566
Superficial SSI, n (%)	1 (1.8)	1 (1.8)	0	1 (4.6)	3 (1.7)	0.648
Hemoperitoneum, n (%)	1 (1.8)	3 (5.3)	0	0	4 (2.3)	0.304
Paralytic ileus (>4 days), n (%)	0	1 (1.8)	0	0	1 (0.6)	0.566
Deep SSI, n (%)	5 (8.7)	2 (3.5)	1 (2.8)	0	8 (4.6)	0.294
Other surgical complications, n (%)	1 (1.8)	0	0	1 (4.6)	2 (1.16)	0.152
Pulmonary complications, n (%)	3 (5.3)	4 (7)	0	0	7 (4)	0.268
Renal complications, n (%)	1 (1.8)	0	0	0	1 (0.6)	0.566
Cardiac complications, n (%)	1 (1.8)	0	0	0	1 (0.6)	0.566
Haematological complications, n (%)	0	2 (3.5)	0	2(9)	4 (2.3)	0.071
Postoperative stay, days, mean, SD	14.10 (12.32)	14.03 (10.95)	14.55 (11.869	11.63 (7.07)		0.592
30-day mortality (%)	4 (7)	2 (3.5)	0	1 (4.6)	7 (4)	0.213

SSI: Surgical Site Infection; Respiratory complications (pneumonia, respiratory failure and pulmonary thromboembolism), Renal complications (hyponatremia, hyperkalaemia, moderate chronic renal failure and acute renal failure), Cardiac complications (atrial fibrillation, arterial hypertension, acute myocardial infarction, heart failure), Haematological complications (anaemia), thrombocytopenia, leukopenia)

Postoperative results

The mean postoperative hospital stay was 13.82 days (SD: 11.14).

Forty-one patients (23.7%) had postoperative complications. Thirty-one patients (17.9%) had surgical complications (anastomotic dehiscence, intestinal obstruction, superficial SSI, deep SSI, hemoperitoneum and paralytic ileus) and ten (5.8%) medical complications (cardiac or hematological, renal, and respiratory). Postoperative complications are described in Table 3.

More severe complications (Clavien Dindo III-IV) occurred in 21 patients (12.14%). Instead, 152 patients (87.86%) were event-free or with less severe complications (Clavien Dindo I-II).

The overall rate of anastomotic dehiscence is 7.56% (13 patients). In patients undergoing left hemicolectomy there were four cases (one in urgency). Of these, three cases underwent resection of the previous anastomosis and Hartman's procedure and one case was treated with coloraffia and lateral ileostomy. This patient developed another anastomotic dehiscence and abdominal compartment syndrome which required multiple operations with open abdomen and delayed closure of the abdomen with Dual mesh.

In patients undergoing segmental colonic resection there were four anastomotic dehiscence (one in urgency). Two were treated surgically: both with anastomotic resection but one with transverse colostomy and one with lateral ileostomy. Two patients were treated conservatively.

In the extended right hemicolectomy group five cases of anastomotic dehiscence (all in urgency). All cases were reoperated with resection of the previous ileo-descendent anastomosis and lateral ileostomy.

The overall rate of intestinal obstruction is 0.6%. The only one patient with intestinal obstruction by infiltrating retroperitoneal mass unidentified in the first surgery that was reoperated with mass resection and jejunal anastomosis.

The rate of superficial SSI (Surgical Site Infections) is 1.7% (three patients). Two of them had complete laparotomic wound dehiscence with reoperation for fascial repair.

The overall rate of hemoperitoneum is 2.6% (four patients). Of these, one was treated conservatively and three reoperated with a splenectomy and two had exploratory laparotomies with evacuation of clots.

A patient with prolonged (>4 days) paralytic ileus was treated conservatively.

The overall rate of deep SSI is 4.6% (eight patients), of which five are patients in the segmental colonic resection group. Of these, one required percutaneous collection drainage and one laparotomic surgery for drainage of abscess and associated anastomotic fistula.

Table 4: Histopathological characteristics.

	Segmental colonic resection (n=57)	Left hemicolectomy (n=57)	Extended right hemicolectomy (n=36)	Total colectomy (n=23)	p value
Lymph nodes harvested, mean, SD	13 (5.28)	14.5 (7.23)	19.3 (8.01)	19.7 (7.01)	0.0001
Lymph nodes n° ≥ 12, n (%)	34 (59.6)	41 (71.9)	35 (97.2)	20 (86.9)	0.0003
T, n (%)					0.405
0	5 (8.7)	2 (3.5)	0	0	
1	3 (5.3)	1 (1.7)	0	0	
2	6 (10.5)	4 (7)	1 (2.8)	1 (4.5)	
3	31 (54.4)	34 (59.6)	25 (69.4)	15 (68.18)	
4a	8 (14)	11 (19.3)	7 (19.4)	6 (27.2)	
4b	4 (7)	5 (8.7)	3 (8.3)	0 (0.0)	
N, n (%)					0.165
0	40 (70.2)	29 (50.8)	19 (52.8)	11 (50)	
1	18 (31.6)	11 (19.3)	9 (25)	6 (27.3)	
2	10 (17.5)	6 (10.5)	8 (22.2)	5 (21.7)	
Stage, n (%)					0.387
0	5 (8.7)	2 (3.5)	0	0	
I	6 (10.5)	5 (8.7)	1 (2.8)	0	
II a	14 (24.6)	23 (40.3)	15 (41.7)	0	
II b	2 (3.5)	7 (12.3)	2 (5.6)	2 (9)	
II c	1 (1.8)	1 (1.8)	1 (2.78)	0	
III a	4 (7)	0	0	0	
III b	15 (26.3)	9 (15.8)	9 (25)	6 (27.3)	
III c	5 (8.7)	5 (8.7)	3 (8.3)	2 (9)	
IV a	3 (5.3)	4 (7)	3 (8.3)	2 (9)	
IV b	2 (3.5)	1 (1.8)	2 (3.5)	2 (9)	

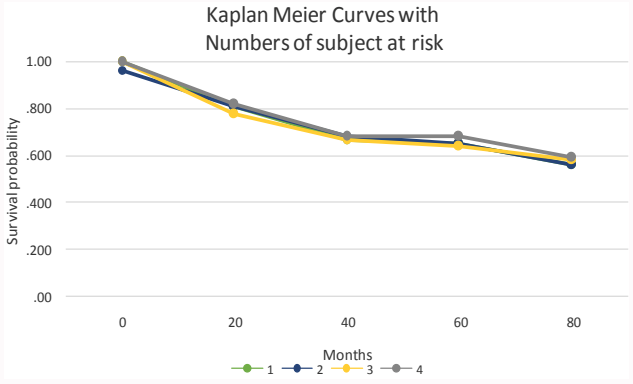

Figure 1: Kaplan Meier Overall Survival (OS) estimates among the four groups. Left hemicolectomy (1, light green line), segmental colonic resection (2, blue line), extended right hemicolectomy (3, yellow line) and total colectomy (4, grey line). The mean 5-year OS is 0.65. No differences between the four groups (log rank test p value =1.08).

The remaining three were treated with antibiotic therapy.

Two patients in the left hemicolectomy group. One treated conservatively and one with reoperation by fascial suture in complete dehiscence also of the laparotomic wound.

The last patient in the extended right hemicolectomy group was treated with antibiotics, evacuation of subcutaneous collections and multiple medications.

Other surgical complications (2 patients, 1.16%) are two pancreatic fistulas, one treated with ERCP (Endoscopic Retrograde colangiopancreatography) and placement of a prosthesis in the Wirsung and one with percutaneous drainage of the collection.

All medical complications are Clavien Dindo type I or II and have been treated conservatively except for one severe hypoxic respiratory failure (Clavien Dindo 4a) which required oxygen and hemodynamic support in intensive care unit.

No statistically significant differences in the various types of complications (surgical or medical) were demonstrated between the four groups.

Histopathological results

Tumour-free surgical resection margins are reported in all definitive histological reports and the distance of the tumour from the proximal and distal margins is always greater than 5 cm. The histopathological results are reported in Table 4.

No significant differences were found between the four groups in terms of T, N and TNM staging 2017 [17]. There is a statistically significant difference between the lymph nodes harvested for a greater number in extended right hemicolectomy and total colectomy. Finally, the segmental colonic resection group contains a number of lymph nodes greater than twelve fewer (p=0.0003) than the other three groups.

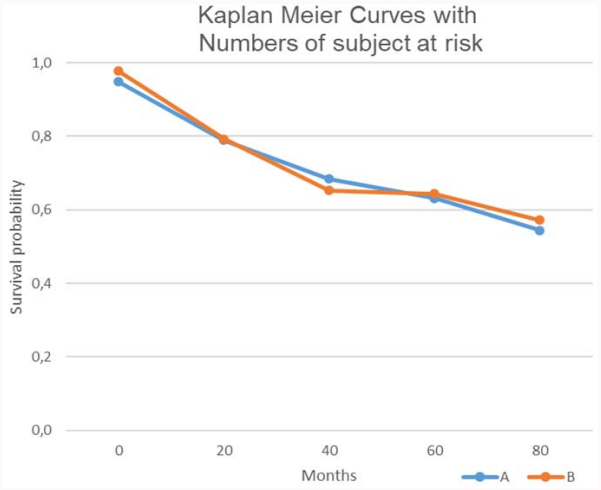

Figure 2: Kaplan Meier Overall Survival (OS) estimates among segmental colonic resection and extended resection. Segmental colonic resection (A, blue line), extended resections (left hemicolectomy and extended right hemicolectomy) (B, red line). No differences between the two arms (log rank test p value =3.55).

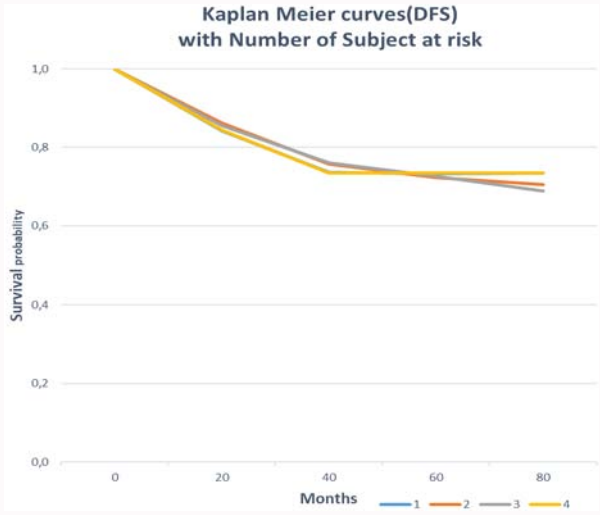

Figure 3: Kaplan Meier Progression Free Survival (PFS) estimates among the four groups. Left hemicolectomy (1, blue line), segmental colonic resection (2, red line), extended right hemicolectomy (3, grey line) and total colectomy (4, yellow line). The yellow and blue lines are almost completely overlapped. The mean 5-year PFS is 0.73. No differences between the four groups (log rank test p value =0.28).

Oncological results

The mean follow-up is 66 months (SD 56.9 months). During the follow-up, 49 relapses and 87 deaths occurred (30 in the segmental colonic resection group, 26 in the left hemicolectomy group, 19 in the right extended hemicolectomy group and 12 in the total colectomy group).

The Overall Survival (OS) does not show significant differences among the four surgical techniques (log rank test p value =1.08) (Figure 1). The mean five-years OS between the four groups is 0.65 (SD 0.02).

The comparison of overall survival between segmental colonic resection and extended resections (extended right hemicolectomy and left hemicolectomy) did not show statistically significant differences (log rank test p value =3.55) (Figure 2).

Regarding the 49 relapses, we found 16 relapses in segmental colonic resection group, 17 in left hemicolectomy group, 10 in extended right hemicolectomy group and 6 in total colectomy group. The Progression Free Survival (PFS) does not show significant differences among the four groups (log rank test p value =0.28) (Figure 3). The mean five-years PFS between the four groups is 0.73 (SD 0.005).

With a univariate and multivariate model, there were no statistically significant differences between the four groups for baseline patient characteristics, intraoperative outcomes, postoperative complications and TNM 2017 staging.

Discussion

At present, there are no recommendations on the extent of surgery to be performed for tumors of the splenic flexure. Hence, there is no optimal surgery and the choice of it depends on several factors. An anonymous survey by members of the Coloproctology Association of Great Britain and Ireland (ACPGBI) showed that extended right hemicolectomy is the preferred option by 63% of respondents followed by left hemicolectomy (23%) and segmental resection of the splenic flexure (14%) [22].

In colorectal cancer surgery, both the extension of the procedure and the surgical dissection of the lymph nodes are established based on the anatomy of the associated vascular structures. From a vascular point of view, the splenic flexure has been described as a “watershed” between the right and left colon with double lymphatic drainage to the superior and inferior mesenteric vessels [23].

A pioneering study by Griffith described that the splenic flexure is vascularized by the terminal branches of the left colic artery in 89% of cases and by the superior mesenteric artery through the middle colic artery in 11% of cases [24].

Further studies confirmed these results by highlighting that the blood flow from the transverse colon has a highly variable anatomy (left branch of the middle colonic artery, artery for the transverse colon, accessory artery for the transverse colon), while the middle colonic artery is completely absent in 20% of cases and a "true" middle colic artery could only be found in 46% of histological specimens [25,26]. More recently, an Accessory Middle Colic Artery (AMCA) running to the splenic flexure has been identified in approximately one third of patients, branching off the superior mesenteric artery in most cases [27].

Using laparoscopic scintigraphic mapping, Vasey et al. found that the lymphatic drainage of the splenic flexure was preferentially directed towards the left colic pedicle with 9.2 time's greater flow than the middle colic pedicle [28].

Nakagoe et al. [29] reported that most lymph node metastases are found along the paracolic arch and left colic artery, while lymph nodes at the root of the middle colic artery and along its left branch are involved in a negligible number of cases (0% and 4.2%, respectively).

Watanabe et al. used peritumoral injection of indocyanine green detecting fluorescence along the accessory middle colic artery towards its origin in all patients with this branch [30].

Currently, the choice between different surgical options is controversial. Notably, a recent multicenter study with a total of 1,304

patients underwent splenic flexure resection or extensive procedures. Segmental resection of splenic flexure showed the same Clavien-Dindo score ≥ 3 postoperative complications (6.44% *vs.* 6.43%, p=0.99), the same 30 days mortality (0.63% *vs.* 0.38%) and comparable long-term outcomes (5-year OS 0.84 *vs.* 0.83, 5-year PFS 0.85 *vs.* 0.84) [20]. Also our study demonstrated comparable overall survival between segmental colonic resection and extended resections.

A recent systematic review of 956 patients from seven observational studies showed that extended right hemicolectomy was associated with more paralytic ileus than left hemicolectomy (OR=2.74, p=0.002) and segmental resection of splenic flexure (OR=6.67, p<0.0001) and operative time was shorter in segmental colonic resection than in extended resections [13]. Furthermore, there are no differences between extended right hemicolectomy, left hemicolectomy, and segmental resection in terms of anastomotic dehiscence, postoperative complications, R0 resection, postoperative mortality, and five-year overall and disease-free survival.

Our study compared the short- and long-term outcomes of the four surgical techniques (segmental colonic resection, extended right hemicolectomy, left hemicolectomy, and total colectomy) in 173 patients with splenic flexure cancer who underwent surgery between September 1998 and March 2020 at two Turin colorectal surgery centers. Patients in our study demonstrated no statistically significant differences in terms of most baseline, intraoperative, postoperative, and TNM stage characteristics. It should be noted, the high number of extended right hemicolectomy and total colectomy (p=0.0001) in urgency due to intestinal obstruction compared to elective setting: this is because these surgical procedures are often necessary due to the presence of considerable distension and impaired colonic perfusion upstream which may also result in diastatic perforation of the cecum.

The only anatomopathological difference between the four groups concerned the number of lymph nodes harvested, significantly higher in the group of patients who underwent extended right hemicolectomy or total colectomy, in consideration of the greater extension of the resection, as in the study by Rega et al. [31]. In particular, in this study, between January 2006 and May 2016, segmental resection with extended or left hemicolectomy in 103 patients with cancer of the splenic flexure at a single center were compared and there is no difference in overall and progression-free survival between the three different surgical treatments.

In our study, there were no statistically significant differences in terms of postoperative complications (overall rate of anastomotic dehiscence, intestinal obstruction, superficial and deep surgical site infections, hemoperitoneum, paralytic ileus and pancreatic fistula) and cancer outcomes (overall survival and progression-free survival) among the four groups. Moreover, there was comparable overall survival between segmental colonic resection and extensive resections (left hemicolectomy and extended right hemicolectomy) (p value 3.55).

A very recent meta-analysis that included 10 non-randomized studies for a total of 2,734 patients reached the same conclusions: it did not show any statistically significant difference between subtotal colectomy, left hemicolectomy, extended right hemicolectomy and segmental colonic resection in terms of rate use of minimally invasive surgery, reoperation, anastomotic dehiscence, mortality, percentage of patients with greater than twelve lymph nodes harvested, local recurrence and overall survival at 5 years [8].

In conclusion, the results obtained after extended right hemicolectomy, left hemicolectomy, segmental colonic resection, and total colectomy in patients with carcinoma of the splenic flexure are comparable.

The highest level of evidence currently available regarding the surgical treatment of splenic flexure cancers derives from meta-analysis of observational studies of moderate quality; therefore, randomized controlled trials with adequate statistical power to provide higher level evidence, to formulate more definitive conclusions, would be desirable. However, considering the rarity of these tumors, it is exceedingly difficult to design and carry out randomized studies in this subgroup of patients.

Conclusion

Segmental colonic resection, extended right hemicolectomy, left hemicolectomy and total colectomy show no significant difference in short-term and oncological outcomes (overall survival e progression free survival) in cancer of the splenic flexure. Moreover, segmental colonic resection has comparable overall survival to extended resections. Further studies with a higher level of evidence are needed.

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