



Emergency surgery for obstructing and perforated colon cancer: patterns of recurrence and prognostic factors

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Abstract

Background The aim of this study was to analyze the incidence, patterns and prognostic factors of recurrence in patients with complicated colon cancer who had emergency surgery within 24 h of admission.

Methods A retrospective observational study was performed on patients with obstructing or perforated colon cancer having resection with curative intent between 1996 and 2014 at a single center. Data were obtained from a prospectively maintained database. Patients who had rectal cancer, iatrogenic endoscopic perforation, stage IV disease, palliative surgery, a colonic stent or decompressive colostomy were excluded.

Results The study included 393 patients. Obstruction was observed in 320 patients (81.4%) and perforation in 73 (18.6%). Hartmann's procedure was more frequently performed by general surgeons (7.5% vs 23.3%; $p = 0.023$). 30-day postoperative mortality was 13.5% (53/393), including 47 (14.7%) obstructed and 6 (8.2%) perforated patients. Postoperative complications (Clavien–Dindo III–IV) occurred in 87 patients (22.1%), including 68 (21.2%) of obstructed and 19 (26.0%) of perforated patients. Anastomotic dehiscence was diagnosed in 52 of 329 (15.8%) patients with primary anastomosis and was higher in the obstructing group than in the perforated group (17.4% vs 7.6%). There was a significantly higher anastomotic dehiscence rate after procedures performed by general surgeons when compared with those performed by colorectal surgeons (10.3% vs 21.3%; $p = 0.005$; OR 2.81, 95% CI 1.4–5.9). With a median follow-up of 6 years, the recurrence rate was 30.1% (67.4% distant, 22.8% local, 9.8% both). Overall and cancer-related survivals were 68.7% and 77.8%, respectively. The presence of positive nodes, male gender, anastomotic dehiscence and diffuse peritonitis were independent predictors for local recurrence while type of surgeon (general) was an independent factor for distant recurrence.

Conclusions Male gender, diffuse peritonitis, positive lymph nodes, type of surgeon and postoperative anastomotic dehiscence significantly influence recurrence of colorectal cancer in this series.

Keywords Perforated colon cancer · Obstructing colon cancer · Emergency surgery · Recurrence · Overall survival · Cancer-related survival · Prognostic factors

Introduction

Approximately, one-third of patients with colorectal cancer present as surgical emergencies, most commonly with perforation (2–10%) and obstruction (8–40%) [1–4]. Emergency surgery for colorectal cancer is associated with a

worse prognosis than elective surgery [2] with 5-year survival rates that range between 12 and 31% in patients with colonic obstruction, and higher rates of cancer recurrence with colonic perforation [5, 6].

However, other data suggest that the outcomes of emergency surgery for colon cancer can improve when adequate treatment with curative oncological criteria is offered and patients are stratified according to tumor stage [7]. As many patients with complicated colon cancer present with evidence of locally advanced or metastatic disease [2, 6], emergency surgery is associated with high rates of postoperative morbidity and mortality. In addition, as emergency operations tend to be of high risk, the emphasis on performing

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curative surgery is not the same as in elective procedures [3, 8].

Some publications report that the outcomes of patients operated on for complicated colon cancer are influenced by several tumor-dependent and surgeon-dependent factors [1, 5, 6]. However, there is a lack of studies that investigate factors that influence local and distant recurrence in this complex patient group. Only retrospective series of heterogeneous populations of patients with colon and rectal cancer have been published. Some of these series include immediate postoperative mortality and may thus overestimate the negative impact of the results [6, 9].

The aim of our study was to determine the incidence, patterns and prognostic factors of recurrence in a single-center cohort of patients with complicated colon cancer requiring emergency surgery. Factors influencing the postoperative complication rate and cancer-specific survival were also analyzed.

Materials and methods

A retrospective observational study was conducted on patients who had emergency surgery for complicated colon cancer (obstructing or perforated) at the Bellvitge University Hospital between January 1996 and December 2014. Data were obtained from a prospectively maintained institutional database and included age, sex, tumor location, type of surgery, hospital stay and postoperative morbidity and mortality. The project received the approval from the Hospital Ethics Committee. The series included data of patients from a prospective study previously published [7].

Patient characteristics

All consecutive patients undergoing radical resection with curative intent were included. Radical resection (R0) was considered when a high ligation of the vascular pedicle was performed, without manipulation of the tumor and partial or complete resection of neighboring organs in the presence of suspected invasion. Surgery was considered curative when there was no macroscopic residual tumor (R2) at the time of surgery and histopathological absence of microscopic tumor invasion of the resection margins (R1). Patients with complicated rectal cancer, iatrogenic perforation after colonoscopy, stage IV disease, palliative surgery a colonic stent or decompressive colostomy were not included in the study. Palliative surgery was indicated when the patient's general condition did not allow adequate local resection. In case of obstruction, a decompressive colostomy was performed. In case of perforation, we performed a terminal ileostomy or colostomy. When the tumor could not be removed due to the presence of locally advanced disease, a bypass was

performed. Colonic stent for obstruction was performed in palliative care patients or in the presence of high postoperative mortality risk (acute renal failure, baseline American Society of Anesthesiologists (ASA) class IV). The extent of intraperitoneal tumor spread and the presence of liver metastases were based on was determined based on the pre-operative and intra-operative evaluations. Emergency surgery was performed within the first 24 h after admission and was indicated in the following situations: clinical signs of obstruction (abdominal distension, nausea, vomiting and absence of flatus or peristalsis for at least 24 h) and radiological confirmation with computed tomography (CT) scan; or perforation (in or near the tumor as well as proximal colonic perforation due to distension), with clinical signs of peritonitis or sepsis and evaluation by abdominal ultrasound or axial CT.

Procedure characteristics and definitions

The operative approach was chosen based on tumor location as previously reported [2]. In patients with proximal tumors and tumors at the splenic flexure, an extended right or right hemi-colectomy with ileocolic anastomosis was performed. In those with tumors distal to the splenic flexure, a left hemi-colectomy was performed. Where possible the preferred operative approach was resection and primary anastomosis with on-table lavage (antegrade or retrograde). On-table antegrade lavage was performed for tumors of the left colon. The cecum was cannulated with a 24-Fr Foley catheter, passed either through the base of the appendix or through an enterotomy in the terminal ileum. The left colon and its mesentery were mobilized outside the abdomen into a plastic bag, and a colotomy was made. Normal saline at 37 °C was used for colonic irrigation. Gentle manipulation of the colon facilitates the lavage. Irrigation was stopped when the effluent was clear. Then the Foley catheter was removed, and the appendix stump or enterotomy was closed. In the retrograde irrigation, a catheter was inserted through a small incision approximately 5 cm proximal to the tumor.

Since 2007, antegrade colonic lavage was only performed if a covering ileostomy was performed to defunction a primary anastomosis. In the rest of patients, a retrograde lavage was performed.

Subtotal colectomy with ileorectal anastomosis was performed when associated damage of the proximal colon (ischemic lesions or perforation due to distension) or a synchronous tumor was observed in the proximal colon. The degree of peritonitis was classified intra-operatively as local or diffuse. In patients with septic shock, fecal peritonitis, failure of several organs or immunocompromised status, a Hartmann procedure or colectomy with terminal ileostomy was performed, depending on the location of the cancer. As an alternative to Hartmann's procedure, primary anastomosis

with a diverting ileostomy was performed in stable patients with associated risk (associated medical problems and corticosteroid treatment).

Surgery was performed by a general surgeon (GS) or a colorectal surgeon (CS).

Asurgeon was considered a CS if, after completing general surgery training, she/he had undergone a training period of at least 2 years at a Colorectal referral center and then working on a daily basis and exclusively in the colorectal unit [10]. Other surgeons were defined as GS.

Postoperative morbidity was classified according to the Clavien–Dindo grading system [11]. Anastomotic dehiscence was defined as generalized or localized peritonitis or discharge of feces, pus, or gas from the abdominal drain or wound. All anastomotic dehiscence was confirmed by one or more of the following methods: an abdominopelvic CT scan, water-soluble contrast enema and laparotomy.

Postoperative mortality was defined as death occurring within 30 days of surgery, or in-hospital death at any time after the operation.

Pathological staging was performed according to the American Joint Committee on Cancer's TNM classification. Histological classification and vascular, lymphatic and perineural invasion were recorded. Unless contraindicated, all patients with stages II and III cancer were treated with adjuvant chemotherapy. During the period studied, the chemotherapy regimen was changing, initially 5-fluorouracil and leucovorin were used, and in 2004, oxaliplatin was added until reaching the current chemotherapy regimen with leucovorin calcium (folinic acid), fluorouracil, and oxaliplatin (FOLFOX). The exclusion criteria for adjuvant chemotherapy were severe medical comorbidities, advanced age, prolonged postoperative stay or patient's refusal.

Patient demographics, tumor characteristics, details of the surgery performed, anastomotic dehiscence, postoperative morbidity and mortality were studied in relation to the mode of presentation (obstruction vs perforation).

Postoperative follow-up

The postoperative follow-up consisted of periodic clinical, laboratory tests, and radiological evaluations, as described in previous publications [2]. Colonoscopy was performed within 2 months of surgery to rule out a synchronous colon tumor not observed intra-operatively. All patients had a minimum of 3 years of follow-up.

Patients who died during the early postoperative period were excluded from the survival analysis.

Local recurrence was defined as tumor at the level of the anastomosis, in the region of primary surgery or in the peritoneum, in all cases confirmed by radiology or histology. Distant recurrence or metastasis was defined as evidence of tumor present beyond the operative site. Overall survival

included all causes of death. The likelihood of being free of recurrence was equivalent to disease-free survival (time from the date of the first treatment until the date of onset of local or distant recurrence). Cancer-specific survival was defined as the time from the date of the first treatment to the date of death as a consequence of the local or distant recurrence of the cancer.

Statistical analysis

Continuous variables are presented as means and standard deviation in brackets or medians and range in brackets. Categorical variables are presented as absolute numbers and in percentages. Comparative analyses of the quantitative data were performed using the Mann–Whitney *U* test. Chi square test for proportions or Fisher's exact tests were used as appropriate.

Univariate and multivariate analyses were performed to identify factors related with severe complications (Clavien–Dindo III–V), anastomotic dehiscence and cancer-specific survival.

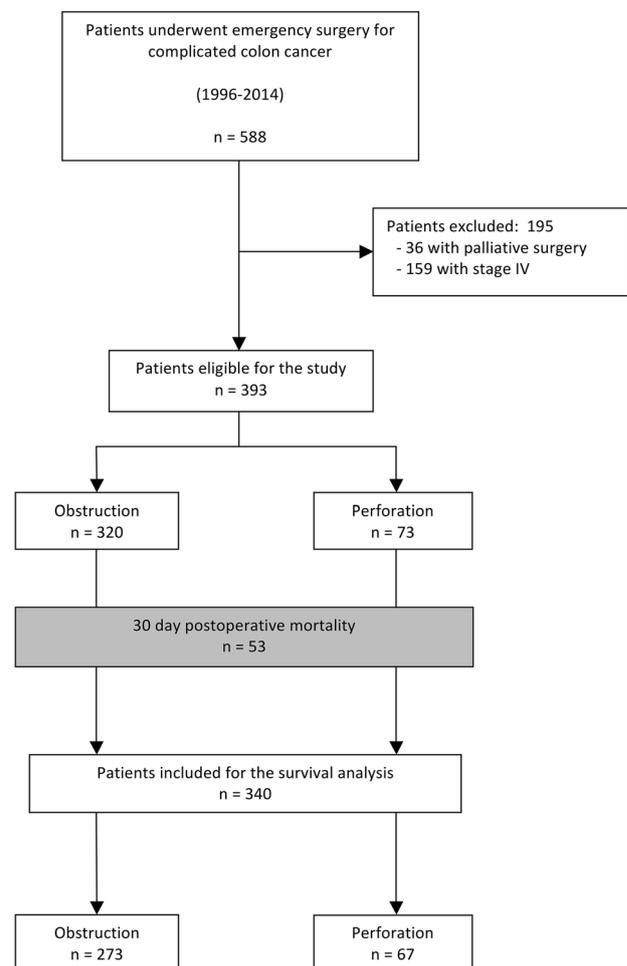


Fig. 1 Flow chart of the study population

Table 1 Demographics and clinicopathological characteristics of patients treated with curative intent

	[ALL] <i>N</i> = 393	Obstruction <i>N</i> = 320	Perforation <i>N</i> = 73	<i>p</i>
Gender				0.737
Female	144 (36.6%)	119 (37.2%)	25 (34.2%)	
Male	249 (63.4%)	201 (62.8%)	48 (65.8%)	
Age (SD)	70.8 [61.0; 79.0]	71.0 [61.7; 79.0]	68.2 [58.3; 75.0]	0.047
ASA score				0.708
I–II	209 (53.2%)	173 (54.1%)	36 (49.3%)	
III	145 (36.9%)	115 (35.9%)	30 (41.1%)	
IV	39 (9.9%)	32 (10.0%)	7 (9.6%)	
Localization				0.815
Proximal	169 (43.0%)	139 (43.4%)	30 (41.1%)	
Distal	224 (57.0%)	181 (56.6%)	43 (58.9%)	
Type of operation				0.001
Right colectomy	155 (39.4%)	129 (40.3%)	26 (35.6%)	
Left colectomy	119 (30.3%)	99 (30.9%)	20 (27.4%)	
Hartmann	41 (10.4%)	24 (7.5%)	17 (23.3%)	
Subtotal colectomy	78 (19.8%)	68 (21.2%)	10 (13.7%)	
Factor surgeon				0.562
CS	187 (47.6%)	155 (48.4%)	32 (43.8%)	
GS	206 (52.4%)	165 (51.6%)	41 (56.2%)	
pT				0.060
pT1–2–3	218 (55.8%)	185 (58.2%)	33 (45.2%)	
pT4	173 (44.2%)	133 (41.8%)	40 (54.8%)	
pN				0.073
pN0	195 (50.1%)	151 (47.8%)	44 (60.3%)	
pN1–2	194 (49.9%)	165 (52.2%)	29 (39.7%)	
Lymphatic invasion				0.320
No	241 (61.3%)	192 (60.0%)	49 (67.1%)	
Yes	152 (38.7%)	128 (40.0%)	24 (32.9%)	
Vascular invasion				0.116
No	280 (71.2%)	222 (69.4%)	58 (79.5%)	
Yes	113 (28.8%)	98 (30.6%)	15 (20.5%)	
Perineural invasion				0.446
No	342 (87.0%)	276 (86.2%)	66 (90.4%)	
Yes	51 (13.0%)	44 (13.8%)	7 (9.6%)	
Lymph nodes < 12 gls				1.000
No	350 (89.1%)	285 (89.1%)	65 (89.0%)	
Yes	43 (10.9%)	35 (10.9%)	8 (11.0%)	
Blood transfusion				0.215
No	222 (56.5%)	186 (58.1%)	36 (49.3%)	
Yes	171 (43.5%)	134 (41.9%)	37 (50.7%)	
Clavien–Dindo				0.074
No	129 (32.8%)	98 (30.6%)	31 (42.5%)	
I–II	124 (31.6%)	107 (33.4%)	17 (23.3%)	
III–IV	87 (22.1%)	68 (21.2%)	19 (26.0%)	
V	53 (13.5%)	47 (14.7%)	6 (8.2%)	
Anastomotic dehiscence				0.111
No	277 (84.2%)	228 (82.6%)	49 (92.5%)	
Yes	52 (15.8%)	48 (17.4%)	4 (7.6%)	
Reintervention				0.502
No	326 (83.0%)	263 (82.2%)	63 (86.3%)	
Yes	67 (17.0%)	57 (17.8%)	10 (13.7%)	

Table 1 (continued)

	[ALL] <i>N</i> = 393	Obstruction <i>N</i> = 320	Perforation <i>N</i> = 73	<i>p</i>
Wound infection				0.626
No	301 (76.6%)	243 (75.9%)	58 (79.5%)	
Yes	92 (23.4%)	77 (24.1%)	15 (20.5%)	
Ileus				0.920
No	335 (85.2%)	272 (85.0%)	63 (86.3%)	
Yes	58 (14.8%)	48 (15.0%)	10 (13.7%)	
Mortality				0.204
No	340 (86.5%)	273 (85.3%)	67 (91.8%)	
Yes	53 (13.5%)	47 (14.7%)	6 (8.2%)	

Kaplan–Meier curves, log-rank test and Cox-proportional hazard regression were performed in univariate analysis to identify potential factors predicting recurrence. All factors with a $p < 0.05$ in univariate analysis or relevant clinic-pathological variables were included as a covariate in multivariate regression analysis to identify independent prognostic factors. A two-tailed $p < 0.05$ was considered statistically significant. Analysis was performed with the statistical software program R version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

For the analysis, patients with obstructing tumors associated with perforation were all included in the obstructing group since perforation was in the proximal colon for distension ischemia.

Results

Between 1996 and 2014, 588 patients had emergency surgery for complicated colon cancer. One-hundred and ninety-five patients were excluded: 36 who had palliative surgery, and 159 who were stage IV, leaving 393 patients for analysis (Fig. 1). Demographic, tumor characteristics, details of the surgery performed and complications in relation to the mode of presentation are reported in Table 1. The initial mode of presentation was obstruction in 320 patients (81.4%) and perforation in 73 (18.6%). Twenty-one patients with obstruction presented diffuse peritonitis due to a cecal perforation caused by severe distention. In 224 patients (57%), the tumor location was distal to the splenic flexure.

There was a significant difference in the type of operation between obstructed and perforated patients ($p = 0.001$). Hartmann's procedure was more frequently performed in the perforation group (7.5% vs 23.3%), while the subtotal colectomy was performed more frequently in the obstructed patients (21.2% vs 13.7%). The number of right colectomies was similar in both groups of patients (35 vs 40%).

23 out of 329 patients (6.9%) with primary anastomosis (21 with obstructed tumor and 2 with perforation) also had

a diverting ileostomy (6 with right colectomy and 17 with left colectomy).

Histopathological investigation revealed that a large proportion of patients had locally advanced disease (T4: 44.2%, N1–2: 49.9%).

Postoperative complications

According to the Clavien–Dindo classification, grades III–IV postoperative complications occurred in 87 patients (22.1%). Among patients that underwent Hartmann's procedure, 46.3% developed severe complications (Clavien–Dindo \geq III) and 24.4% died during the postoperative period. Table 2 reports univariate and multivariate analyses of predictive factors for postoperative complications for obstructing and perforated cancers separately. In the univariate analysis of both groups, the presence of diffuse peritonitis, due to cancer perforation or to proximal colonic perforation for distention, was related to postoperative severe complications. In the multivariate analysis, male gender and blood transfusion were predictive factors for severe postoperative complications (Clavien–Dindo III–V) both in obstructing and perforated colon cancers, while ASA class was independently related with complications only in the presence of obstructing cancers.

Anastomotic dehiscence

Anastomotic dehiscence occurred in 52 patients out of 329 (15.8%) with primary anastomosis, with 35 patients (10.6%) requiring reinterventions. The anastomotic dehiscence rate was higher but without reaching statistical significance in right colectomy when compared with distal resection (18.2% vs 15.8%; $p = 0.609$; OR 0.84, 95% CI 0.4–1.62). Colorectal specialization was related with a significantly lower anastomotic dehiscence rate when compared with general surgery training (10.3% vs 21.3%; $p = 0.005$; OR 2.81, 95% CI 1.4–5.9). Male gender, the presence of obstructing cancer, general surgeon and pT4 tumors were independent factors

Table 2 Univariate and multivariate analyses of prognostic variables for complications (Clavien–Dindo III–V) in the two groups

	Obstruction			Perforation			Multivariate			Univariate			Multivariate		
	N = 115/320	OR CI 95%	p ratio	N = 25/73	OR CI 95%	p ratio	OR CI 95%	p ratio	OR CI 95%	p ratio	OR CI 95%	p ratio	OR CI 95%	p ratio	
Gender															
Female	36 (30.3%)	Ref.	Ref.	4 (16.0%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
Male	79 (39.3%)	1.49 [0.92; 2.43]	0.104	21 (43.8%)	3.92 [1.24; 15.5]	0.026	1.81 (1.08; 3.07)	0.018	3.92 [1.24; 15.5]	0.018	10.92 (2.81; 53.71)	0.001	10.92 (2.81; 53.71)	0.001	
Age (SD)	72.8 (11.4)	1.03 [1.01; 1.06]	0.002	69.2 (13.1)	1.02 [0.99; 1.06]			0.194	1.02 [0.99; 1.06]						
ASA score															
I–II	45 (26.0%)	Ref.	Ref.	10 (27.8%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
III	53 (46.1%)	2.42 [1.47; 4.01]	< 0.001	9 (30.0%)	1.11 [0.37; 3.31]	0.001	2.32 (1.39; 3.89)	0.846	1.11 [0.37; 3.31]	0.846					
IV	17 (53.1%)	3.20 [1.47; 7.05]	0.004	6 (85.7%)	13.2 [1.86; 373]	0.005	3.16 (1.42; 7.09)	0.007	13.2 [1.86; 373]	0.007					
Peritonitis															
No	94 (34.4%)	Ref.	Ref.	9 (22.5%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
Localized	8 (30.8%)	0.86 [0.34; 2.00]	0.725	16 (48.5%)	3.17 [1.17; 9.10]	0.016		0.023	3.17 [1.17; 9.10]	0.023					
Diffuse	13 (61.9%)	3.06 [1.23; 8.08]	0.016												
Type of operation															
Right colectomy	46 (35.7%)	Ref.	Ref.	8 (30.8%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
Left colectomy	28 (28.3%)	0.71 [0.40; 1.26]	0.243	6 (30.0%)	0.97 [0.26; 3.52]	0.243		0.961	0.97 [0.26; 3.52]	0.961					
Hartmann	11 (45.8%)	1.52 [0.62; 3.72]	0.355	8 (47.1%)	1.96 [0.54; 7.30]	0.355		0.304	1.96 [0.54; 7.30]	0.304					
Subtotal colectomy	30 (44.1%)	1.42 [0.78; 2.60]	0.252	3 (30.0%)	0.98 [0.17; 4.79]	0.252		0.983	0.98 [0.17; 4.79]	0.983					
Factor surgeon															
CS	49 (31.6%)	Ref.	Ref.	10 (31.2%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
GS	66 (40.0%)	1.44 [0.91; 2.29]	0.120	15 (36.6%)	1.26 [0.47; 3.48]	0.120		0.646	1.26 [0.47; 3.48]	0.646					
pT															
pT1–2–3	60 (32.4%)	Ref.	Ref.	10 (30.3%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
pT4	55 (41.4%)	1.47 [0.92; 2.34]	0.105	15 (37.5%)	1.37 [0.51; 3.77]	0.105		0.533	1.37 [0.51; 3.77]	0.533					
pN															
pN0	54 (35.8%)	Ref.	Ref.	18 (40.9%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
pN1–2	59 (35.8%)	1.00 [0.63; 1.59]	0.999	7 (24.1%)	0.47 [0.15; 1.31]	0.999		0.150	0.47 [0.15; 1.31]	0.150					
Transfusion															
No	50 (26.9%)	Ref.	Ref.	6 (16.7%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	
Yes	65 (48.5%)	2.55 [1.60; 4.10]	< 0.001	19 (51.4%)	5.08 [1.77; 16.5]	< 0.001	2.77 (1.69; 4.58)	< 0.001	5.08 [1.77; 16.5]	0.002	12.05 (3.49; 50.13)	< 0.001	12.05 (3.49; 50.13)	< 0.001	

Table 3 Univariate and multivariate analyses of prognostic variables for anastomotic dehiscence

	[ALL] <i>N</i> = 329	Yes <i>N</i> = 52	Univariate		Multivariate	
			OR CI 95%	<i>p</i> ratio	OR CI 95%	<i>p</i> ratio
Gender						
Female	119 (36.2%)	11 (9.2%)	Ref.	Ref.	Ref.	Ref.
Male	210 (63.8%)	41 (19.5%)	2.35 [1.19; 5.02]	0.013	2.51 (1.25; 5.41)	0.013
Age (SD)	68.2 (11.9)	69.7 (11.8)	1.01 [0.99; 1.04]	0.344		
ASA score						
I–II	187 (56.8%)	26 (13.9%)	Ref.	Ref.		
III	114 (34.7%)	25 (21.9%)	1.74 [0.94; 3.20]	0.077		
IV	28 (8.5%)	1 (3.6%)	0.26 [0.01; 1.31]	0.118		
Initial presentation						
Perforation	53 (16.1%)	4 (7.6%)	Ref.	Ref.	Ref.	Ref.
Obstruction	276 (83.9%)	48 (17.4%)	2.49 [0.95; 8.74]	0.064	3.00 (1.13; 10.46)	0.047
Peritonitis						
No	242 (73.6%)	43 (17.8%)	Ref.	Ref.		
Localized	55 (16.7%)	6 (10.9%)	0.58 [0.21; 1.35]	0.219		
Diffuse	32 (9.73%)	3 (9.38%)	0.50 [0.11; 1.51]	0.239		
Type of operation						
Right colectomy	148 (45.0%)	27 (18.2%)	Ref.	Ref.		
Left colectomy	114 (34.7%)	18 (15.8%)	0.84 [0.43; 1.62]	0.609		
Subtotal colectomy	67 (20.4%)	7 (10.4%)	0.53 [0.20; 1.24]	0.149		
Factor surgeon						
CS	165 (50.2%)	17 (10.3%)	Ref.	Ref.	Ref.	Ref.
GS	164 (49.8%)	35 (21.3%)	2.35 [1.27; 4.49]	0.006	2.74 (1.46; 5.35)	0.002
pT						
pT1–2–3	186 (56.7%)	24 (12.9%)	Ref.	Ref.	Ref.	Ref.
pT4	142 (43.3%)	28 (19.7%)	1.65 [0.91; 3.03]	0.099	1.93 (1.04; 3.61)	0.039
Transfusion						
No	196 (59.6%)	26 (13.3%)	Ref.	Ref.		
Yes	133 (40.4%)	26 (19.5%)	1.59 [0.87; 2.89]	0.131		

significantly influencing the anastomotic dehiscence rate (Table 3). The 30-day postoperative mortality rate was 13.5% (53/393). When obstructed and perforated cancers were examined separately, it was found that male gender and general surgeon (GS) were independent factors that significantly influenced in the anastomotic dehiscence in patients with obstruction. Since only four patients with perforation presented a dehiscence, a multivariate analysis was not possible (Table 4).

Results by surgical speciality

Of all the series, 187 (47.6%) patients were operated on by CS and 206 (52.4%) patients by GS. Differences were observed in anastomotic dehiscence ($p=0.01$) and the distribution of the types of operation according to the two groups of surgeons ($p=0.015$). CS and GS performed, respectively, left colectomy with primary anastomosis in 68 (36.4%) and

51 (24.8%) patients, Hartmann's operation in 12 (6.4%) and 29 (14.1%) patients. In comparison with CS, GS performed more Hartmann's procedures than left colectomy with primary anastomosis ($p=0.023$) (Table 5).

Adjuvant therapy and cancer-specific survival

After exclusion of patients who died in the postoperative period, 340 patients were included in the survival analysis with a median follow-up of 6 years (range 2.8–10.6 years). It was observed that ASA grade ($p<0.001$), associated severe medical problems (heart disease, chronic obstructive pulmonary disease, renal insufficiency, liver disease, chronic treatment with corticosteroids and anemia) ($p=0.001$), anastomotic dehiscence ($p=0.001$), length of hospital stay ($p<0.001$), and need for reoperation ($p=0.045$) were factors that significantly influenced the decision to not administrate

Table 4 Univariate and multivariate analyses of prognostic variables for anastomotic dehiscence in patients with obstruction and perforation

	Obstruction			Perforation				
	Univariate		<i>p</i> ratio	Multivariate		Univariate		
	<i>N</i> =48/320	OR CI 95%		OR CI 95%	<i>p</i> ratio	<i>N</i> =4/73	OR CI 95%	<i>p</i> ratio
Gender								
Female	10 (10.1%)	Ref.	Ref.			1 (5.00%)	Ref.	Ref.
Male	38 (21.5%)	2.40 [1.17; 5.35]	0.015	2.55 (1.24; 5.69)	0.015	3 (9.09%)	1.74 [0.19; 52.5]	0.652
Age (SD)	69.0 (11.7)	1.00 [0.97; 1.03]	0.911			78.2 (12.0)	1.14 [1.01; 1.28]	0.035
ASA score								
I–II	24 (15.2%)	Ref.	Ref.			2 (6.90%)	Ref.	Ref.
III	23 (24.5%)	1.80 [0.95; 3.44]	0.073			2 (10.0%)		
IV	1 (4.17%)	0.28 [0.01; 1.42]	0.143			0 (0.00%)		
Peritonitis								
No	43 (17.8%)	Ref.	Ref.					
Localized	4 (19.0%)	1.12 [0.30; 3.24]	0.851			2 (5.88%)	Ref.	Ref.
Diffuse	1 (7.69%)	0.44 [0.02; 2.33]	0.389			2 (10.5%)	1.86 [0.18; 19.2]	0.579
Type of operation								
Right colectomy	24 (19.5%)	Ref.	Ref.			3 (12.0%)	Ref.	Ref.
Left colectomy	17 (18.1%)	0.91 [0.45; 1.82]	0.797			1 (5.00%)		
Subtotal colectomy	7 (11.9%)	0.56 [0.21; 1.35]	0.205			0 (0.00%)		
Factor surgeon								
CS	16 (11.3%)	Ref.	Ref.			1 (4.17%)	Ref.	Ref.
GS	32 (23.7%)	2.41 [1.26; 4.75]	0.007	2.52 (1.32; 5.00)	0.006	3 (10.3%)	2.41 [0.26; 72.7]	0.462
pT								
pT1–2–3	23 (14.3%)	Ref.	Ref.			1 (4.00%)	Ref.	Ref.
pT4	25 (21.9%)	1.68 [0.90; 3.17]	0.106			3 (10.7%)	2.61 [0.28; 78.8]	0.420
Transfusion								
No	24 (14.2%)	Ref.	Ref.			2 (7.41%)	Ref.	Ref.
Yes	24 (22.4%)	1.74 [0.93; 3.28]	0.085			2 (7.69%)	1.04 [0.10; 10.7]	0.971

adjuvant chemotherapy. Therefore, adjuvant chemotherapy was administered in only 55% (187/340) of patients with stage II (50.6%) and stage III (62.3%) disease. 92 patients (30.1%) had radiological or histological evidence of recurrence, while the overall survival and cancer-specific survival rates at 5 years were 68.7% (95% CI 63.8–73.9) and 77.8% (95% CI 73.3–82.7), respectively. Male gender, age, presence of diffuse peritonitis, positive nodes and vascular invasion were independent predictive factors for cancer-specific survival (Tables 6), while male gender, age and vascular invasion were predictive factors for overall survival (Table 7). Age was the only significant predictive factor for cancer-specific survival and overall survival in the presence of perforated cancer

when patients with obstruction and perforation were analyzed separately, probably due to the low number of events. However, for obstructing tumors, male gender, age, ASA grade IV, associated diffuse peritonitis, positive lymph nodes and vascular invasion continued being significant (Tables 8, 9).

Site of recurrence

Recurrence was distant in 62 patients (67.4%), local in 13 (14.1%), and local and distant in 8 (8.7%). The most frequent site was the liver, followed by the lung and other locations. Recurrence in the form of carcinomatosis occurred in 9 patients (9.8%). Local recurrence was higher

Table 5 Demographics and clinicopathological characteristics of patients based on type of surgeon

	[ALL] N= 393	CS N= 187	GS N= 206	p value
Gender				
Female	144 (36.6%)	66 (35.3%)	78 (37.9%)	0.672
Male	249 (63.4%)	121 (64.7%)	128 (62.1%)	
Age (SD)	69.5 (12.1)	68.8 (11.4)	70.0 (12.6)	0.323
ASA score				
I–II	209 (53.2%)	104 (55.6%)	105 (51.0%)	0.448
III	145 (36.9%)	63 (33.7%)	82 (39.8%)	
IV	39 (9.92%)	20 (10.7%)	19 (9.22%)	
Initial presentation				
Obstruction	320 (81.4%)	155 (82.9%)	165 (80.1%)	0.562
Perforation	73 (18.6%)	32 (17.1%)	41 (19.9%)	
Peritonitis				
No	273 (69.5%)	133 (71.1%)	140 (68.0%)	0.381
Localized	66 (16.8%)	33 (17.6%)	33 (16.0%)	
Diffuse	54 (13.7%)	21 (11.2%)	33 (16.0%)	
Type of operation				0.015
Right colectomy	155 (39.4%)	69 (36.9%)	86 (41.7%)	
Left colectomy	119 (30.3%)	68 (36.4%)	51 (24.8%)	
Hartmann	41 (10.4%)	12 (6.42%)	29 (14.1%)	
Subtotal colectomy	78 (19.8%)	38 (20.3%)	40 (19.4%)	
Site of tumor				
Proximal	169 (43.0%)	79 (42.2%)	90 (43.7%)	0.852
Distal	224 (57.0%)	108 (57.8%)	116 (56.3%)	
pT				
pT1–2–3	218 (55.5%)	218 (55.8%)	98 (52.4%)	0.240
pT4	175 (44.5%)	89 (49.1%)	89 (50.9%)	
pN				
pN0	195 (50.1%)	93 (50.3%)	102 (50.0%)	1.000
pN1–2	194 (49.9%)	92 (49.7%)	102 (50.0%)	
Lymph nodes resected < 12				
No	350 (89.1%)	167 (89.3%)	183 (88.8%)	1.000
Yes	43 (10.9%)	20 (10.7%)	23 (11.2%)	
Wound infection				
No	301 (76.6%)	137 (73.3%)	164 (79.6%)	0.172
Yes	92 (23.4%)	50 (26.7%)	42 (20.4%)	
Transfusion				
No	222 (56.5%)	111 (59.4%)	111 (53.9%)	0.321
Yes	171 (43.5%)	76 (40.6%)	95 (46.1%)	
Chemotherapy				
No	206 (52.4%)	88 (47.1%)	118 (57.3%)	0.054
Yes	187 (47.6)	99 (52.9%)	88 (42.7%)	
Clavien–Dindo				
No	129 (32.8%)	57 (30.5%)	72 (35.0%)	0.068
I–II	124 (31.6%)	71 (38.0%)	53 (25.7%)	
III–IV	87 (22.1%)	38 (20.3%)	49 (23.8%)	
V	53 (13.5%)	21 (11.2%)	32 (15.5%)	
Anastomotic dehiscence				
No	277 (84.2%)	148 (89.7%)	129 (78.7%)	0.010
Yes	52 (15.8%)	17 (10.3%)	35 (21.3%)	
Proximal				

Table 5 (continued)

	[ALL] N= 393	CS N= 187	GS N= 206	<i>p</i> value
No	131 (84.5%)	67 (93.1%)	64 (77.1%)	0.012
Yes	24 (15.5%)	5 (6.94%)	19 (22.9%)	
Distal				
No	146 (83.9%)	81 (87.1%)	65 (80.2%)	0.308
Yes	28 (16.1%)	12 (12.9%)	16 (19.8%)	
Reoperation				
No	326 (83.0%)	157 (84.0%)	169 (82.0%)	0.711
Yes	67 (17.0%)	30 (16.0%)	37 (18.0%)	
Postoperative death				
No	340 (86.5%)	166 (88.8%)	174 (84.5%)	0.271
Yes	53 (13.5%)	21 (11.2%)	32 (15.5%)	

CS colorectal surgeon, GS general surgeon

in patients with perforation than in those with obstruction (20.8% vs 11.8%). However, no significant differences were found between the form of presentation and the site of recurrence (Table 10).

Time to recurrence

In 62 (67.4%) out of 92 patients, recurrence occurred within 2 years of surgery, while in the other 30 patients (32.6%) it was diagnosed in the following years. Distant recurrence (69.4%, 43 patients) was the most frequent form during the first 2 years (liver = 17, lung = 15, other = 11). Factors such as type of presentation (obstruction or perforation), advanced stage (T4, N+) or adjuvant treatment did not significantly influence the time of onset of recurrence ($p=0.781$, $p=0.085$ and $p=0.168$, respectively) (Fig. 2).

Prognostic factors for recurrence

The univariate analysis showed that overall recurrence was significantly associated with male gender, diffuse peritonitis, lymphatic invasion, vascular invasion, and the presence of positive lymph nodes (Table 11). A multivariate analysis in which all these variables and other clinically relevant factors were included detected independent predictors both for overall recurrence and for local and distant recurrence (Table 12). Positive nodes and diffuse peritonitis showed a

strong association with recurrence in general and with local and distant recurrence. Similarly, male gender was associated with both overall recurrence and distant recurrence. Type of surgeon (GS) was an independent prognostic factor for distant recurrence, while anastomotic dehiscence was independent predictor of local recurrence.

Discussion

The present study shows that recurrence in patients with complicated colon cancer who undergo emergency surgery recurrence occurs more frequently during the first 2 years after surgery, with distant metastases being the most frequent location. Male gender, diffuse peritonitis, positive lymph nodes, anastomotic dehiscence and type of surgeon were all prognostic factors for recurrence.

One of the main strengths of this study is that it was carried out at a tertiary referral center by specialists in coloproctology, where the management protocol has been in place for many years under the control of the same surgeon. In our unit, emergency surgery for colon cancer is always attempted with curative intent in suitable patients, and achieves survival figures close to those of elective surgery [2, 7, 12]. Patients that died in the immediate postoperative period were deliberately removed from the survival analysis, as their inclusion in many series constitutes a bias when evaluating the long-term oncological results.

This study has limitations: despite the prospective collection of data, patients were enrolled over an 18-year period

Table 6 Univariate and multivariate analyses of prognostic variables for cancer-specific survival

	[ALL] <i>N</i> = 340	No event <i>N</i> = 257	Event <i>N</i> = 83	Univariate		Multivariate	
				HR CI 95%	<i>p</i> value	HR CI 95%	<i>p</i> value
Gender							
Female	128 (37.6%)	102 (79.7%)	26 (20.3%)	Ref.	Ref.	Ref.	Ref.
Male	212 (62.4%)	155 (73.1%)	57 (26.9%)	1.48 [0.93; 2.35]	0.098	1.76 (1.10; 2.84)	0.019
Age (SD)	68.1 (11.9)	67.6 (11.8)	69.5 (12.0)	1.02 [1.01; 1.04]	0.012	1.03 (1.01; 1.05)	0.006
ASA score							
I–II	195 (57.4%)	151 (77.4%)	44 (22.6%)	Ref.	Ref.		
III	125 (36.8%)	90 (72.0%)	35 (28.0%)	1.58 [1.01; 2.47]	0.044		
IV	20 (5.88%)	16 (80.0%)	4 (20.0%)	1.31 [0.47; 3.65]	0.607		
Site of tumor							
Proximal	144 (42.4%)	104 (72.2%)	40 (27.8%)	Ref.	Ref.		
Distal	196 (57.6%)	153 (78.1%)	43 (21.9%)	0.74 [0.48; 1.15]	0.181		
Initial presentation							
Obstruction	273 (80.3%)	209 (76.6%)	64 (23.4%)	Ref.	Ref.		
Perforation	67 (19.7%)	48 (71.6%)	19 (28.4%)	1.07 [0.64; 1.79]	0.792		
Peritonitis							
No	235 (69.1%)	183 (77.9%)	52 (22.1%)	Ref.	Ref.	Ref.	Ref.
Localized	64 (18.8%)	48 (75.0%)	16 (25.0%)	1.07 [0.61; 1.88]	0.804	1.18 (0.67; 2.09)	0.560
Diffuse	41 (12.1%)	26 (63.4%)	15 (36.6%)	1.65 [0.93; 2.94]	0.087	2.14 (1.19; 3.86)	0.011
Factor surgeon							
CS	166 (48.8%)	133 (80.1%)	33 (19.9%)	Ref.	Ref.		
GS	174 (51.2%)	124 (71.3%)	50 (28.7%)	1.39 [0.90; 2.16]	0.142		
pT							
pT1–2–3	194 (57.4%)	153 (78.9%)	41 (21.1%)	Ref.	Ref.		
pT4	144 (42.6%)	102 (70.8%)	42 (29.2%)	1.61 [1.04; 2.47]	0.032		
pN							
pN0	171 (50.6%)	144 (84.2%)	27 (15.8%)	Ref.	Ref.	Ref.	Ref.
pN1–2	167 (49.4%)	111 (66.5%)	56 (33.5%)	2.48 [1.57; 3.93]	< 0.001	2.39 (1.48; 3.87)	< 0.001
Lymphatic invasion							
No	212 (62.4%)	172 (81.1%)	40 (18.9%)	Ref.	Ref.		
Yes	128 (37.6%)	85 (66.4%)	43 (33.6%)	1.99 [1.29; 3.06]	0.002		
Vascular invasion							
No	245 (72.1%)	197 (80.4%)	48 (19.6%)	Ref.	Ref.	Ref.	Ref.
Yes	95 (27.9%)	60 (63.2%)	35 (36.8%)	2.27 [1.46; 3.52]	< 0.001	1.92 (1.21; 3.03)	0.005
Perineural invasion							
No	294 (86.5%)	228 (77.6%)	66 (22.4%)	Ref.	Ref.		
Yes	46 (13.5%)	29 (63.0%)	17 (37.0%)	2.05 [1.20; 3.50]	0.009		
Lymph nodes < 12							
No	306 (90.0%)	233 (76.1%)	73 (23.9%)	Ref.	Ref.		
Yes	34 (10.0%)	24 (70.6%)	10 (29.4%)	1.19 [0.61; 2.32]	0.608		
Chemotherapy							
No	153 (45.0%)	115 (75.2%)	38 (24.8%)	Ref.	Ref.		
< 2004	84 (24.7%)	65 (77.4%)	19 (22.6%)	0.65 [0.37; 1.15]	0.137		
≥ 2004	103 (30.3%)	77 (74.8%)	26 (25.2%)	0.92 [0.56; 1.52]	0.751		

Table 7 Univariate and multivariate analyses of prognostic variables for overall survival

	[ALL] <i>N</i> = 340	No event <i>N</i> = 180	Event <i>q</i> = 160	Univariate		Multivariate	
				HR CI 95%	<i>p</i> ratio	HR CI 95%	<i>p</i> ratio
Gender							
Female	128 (37.6%)	79 (61.7%)	49 (38.3%)	Ref.	Ref.	Ref.	Ref.
Male	212 (62.4%)	101 (47.6%)	111 (52.4%)	1.58 [1.13; 2.22]	0.008	1.76 (1.25; 2.47)	0.001
Age (SD)	68.1 (11.9)	65.2 (11.8)	71.2 (11.2)	1.05 [1.03; 1.06]	< 0.001	1.05 (1.03; 1.06)	< 0.001
ASA score							
I–II	195 (57.4%)	116 (59.5%)	79 (40.5%)	Ref.	Ref.		
III	125 (36.8%)	56 (44.8%)	69 (55.2%)	2.00 [1.44; 2.78]	< 0.001		
IV	20 (5.88%)	8 (40.0%)	12 (60.0%)	2.32 [1.26; 4.27]	0.007		
Site of tumor							
Proximal	144 (42.4%)	69 (47.9%)	75 (52.1%)	Ref.	Ref.		
Distal	196 (57.6%)	111 (56.6%)	85 (43.4%)	0.75 [0.55; 1.02]	0.071		
Initial presentation							
Obstruction	273 (80.3%)	145 (53.1%)	128 (46.9%)	Ref.	Ref.		
Perforation	67 (19.7%)	35 (52.2%)	32 (47.8%)	0.85 [0.58; 1.26]	0.419		
Peritonitis							
No	235 (69.1%)	126 (53.6%)	109 (46.4%)	Ref.	Ref.		
Localized	64 (18.8%)	37 (57.8%)	27 (42.2%)	0.90 [0.59; 1.37]	0.617		
Diffuse	41 (12.1%)	17 (41.5%)	24 (58.5%)	1.21 [0.78; 1.88]	0.402		
Factor surgeon							
CS	166 (48.8%)	90 (54.2%)	76 (45.8%)	Ref.	Ref.		
GS	174 (51.2%)	90 (51.7%)	84 (48.3%)	0.91 [0.67; 1.25]	0.578		
pT							
pT1–2–3	194 (57.4%)	101 (52.1%)	93 (47.9%)	Ref.	Ref.		
pT4	144 (42.6%)	78 (54.2%)	66 (45.8%)	1.21 [0.88; 1.66]	0.248		
pN							
pN0	171 (50.6%)	92 (53.8%)	79 (46.2%)	Ref.	Ref.		
pN1–2	167 (49.4%)	87 (52.1%)	80 (47.9%)	1.23 [0.90; 1.68]	0.193		
Lymphatic invasion							
No	212 (62.4%)	116 (54.7%)	96 (45.3%)	Ref.	Ref.		
Yes	128 (37.6%)	64 (50.0%)	64 (50.0%)	1.24 [0.90; 1.70]	0.181		
Vascular invasion							
No	245 (72.1%)	140 (57.1%)	105 (42.9%)	Ref.	Ref.	Ref.	Ref.
Yes	95 (27.9%)	40 (42.1%)	55 (57.9%)	1.77 [1.27; 2.46]	0.001	1.81 (1.30; 2.53)	< 0.001
Perineural invasion							
No	294 (86.5%)	158 (53.7%)	136 (46.3%)	Ref.	Ref.		
Yes	46 (13.5%)	22 (47.8%)	24 (52.2%)	1.57 [1.01; 2.43]	0.044		
Lymph nodes < 12							
No	306 (90.0%)	167 (54.6%)	139 (45.4%)	Ref.	Ref.		
Yes	34 (10.0%)	13 (38.2%)	21 (61.8%)	1.25 [0.79; 1.98]	0.344		
Chemotherapy							
No	153 (45.0%)	65 (42.5%)	88 (57.5%)	Ref.	Ref.		
< 2004	84 (24.7%)	48 (57.1%)	36 (42.9%)	0.42 [0.28; 0.63]	< 0.001		
≥ 2004	103 (30.3%)	67 (65.0%)	36 (35.0%)	0.61 [0.41; 0.90]	0.012		

Table 8 Univariate and multivariate analyses of prognostic variables for cancer-specific survival

	Obstruction		Univariate		Multivariate		Perforation		Univariate		Multivariate	
	Event N = 64/273	HR CI 95%	p value	HR CI 95%	p value	Event N = 19/67	HR CI 95%	p value	HR CI 95%	p value		
Gender												
Female	20 (19.4%)	Ref.	Ref.			6 (24.0%)	Ref.	Ref.				
Male	44 (25.9%)	1.49 [0.88; 2.53]	0.138			13 (31.0%)	1.42 [0.54; 3.75]	0.482				
Age (SD)	69.1 (12.5)	1.01 [0.99; 1.04]	0.223			71.0 (10.5)	1.06 [1.01; 1.10]	0.007			1.06 [1.01; 1.10]	0.007
ASA score												
I–II	33 (20.8%)	Ref.	Ref.			11 (30.6%)	Ref.	Ref.				
III	29 (29.9%)	1.90 [1.15; 3.14]	0.012			6 (21.4%)	0.75 [0.27; 2.02]	0.563				
IV	2 (11.8%)	0.89 [0.21; 3.72]	0.873			2 (66.7%)	2.26 [0.50; 10.2]	0.291				
Site of tumor												
Proximal	33 (28.2%)	Ref.	Ref.			7 (25.9%)	Ref.	Ref.				
Distal	31 (19.9%)	0.68 [0.42; 1.11]	0.125			12 (30.0%)	0.93 [0.36; 2.42]	0.878				
Peritonitis												
No	52 (22.1%)	Ref.	Ref.									
Localized	6 (25.0%)	1.09 [0.47; 2.53]	0.849			10 (25.0%)	Ref.	Ref.				
Diffuse	6 (42.9%)	2.74 [1.17; 6.40]	0.020			9 (33.3%)	1.08 [0.42; 2.75]	0.878				
Factor surgeon												
CS	28 (20.6%)	Ref.	Ref.			5 (16.7%)	Ref.	Ref.				
GS	36 (26.3%)	1.26 [0.77; 2.07]	0.361			14 (37.8%)	1.98 [0.70; 5.58]	0.197				
pT												
pT1–2–3	34 (20.9%)	Ref.	Ref.			7 (22.6%)	Ref.	Ref.				
pT4	30 (27.8%)	1.52 [0.93; 2.49]	0.098			12 (33.3%)	1.82 [0.70; 4.72]	0.220				
pN												
pN0	19 (14.4%)	Ref.	Ref.			8 (20.5%)	Ref.	Ref.				
pN1–2	45 (32.4%)	2.66 [1.55; 4.54]	< 0.001			11 (39.3%)	2.09 [0.84; 5.22]	0.112				
Lymphatic invasion												
No	26 (15.6%)	Ref.	Ref.			14 (31.1%)	Ref.	Ref.				
Yes	38 (35.8%)	2.71 [1.64; 4.46]	< 0.001			5 (22.7%)	0.65 [0.23; 1.81]	0.409				
Vascular invasion												
No	33 (17.3%)	Ref.	Ref.			15 (27.8%)	Ref.	Ref.				
Yes	31 (37.8%)	2.69 [1.64; 4.41]	< 0.001			4 (30.8%)	1.07 [0.35; 3.26]	0.903				
Perineural invasion												
No	49 (20.9%)	Ref.	Ref.			17 (28.3%)	Ref.	Ref.				
Yes	15 (38.5%)	2.27 [1.27; 4.05]	0.006			2 (28.6%)	1.14 [0.26; 4.96]	0.862				
Lymph nodes < 12												
No	55 (22.5%)	Ref.	Ref.			18 (29.0%)	Ref.	Ref.				
Yes	9 (31.0%)	1.38 [0.68; 2.79]	0.377			1 (20.0%)	0.46 [0.06; 3.75]	0.469				

Table 8 (continued)

	Obstruction Event N = 64/273	Univariate		Multivariate		Perforation Event N = 19/67	Univariate		Multivariate	
		HR	CI 95%	p value	HR		CI 95%	HR	CI 95%	p value
Chemotherapy										
No	29 (22.8%)	Ref.	Ref.	Ref.	Ref.	9 (34.6%)	Ref.	Ref.	Ref.	Ref.
<2004	13 (21.0%)	0.69 [0.35; 1.34]	0.272	0.69 [0.35; 1.34]	0.272	6 (27.3%)	0.55 [0.19; 1.59]	0.274	0.55 [0.19; 1.59]	0.274
≥2004	22 (26.2%)	1.01 [0.58; 1.75]	0.980	1.01 [0.58; 1.75]	0.980	4 (21.1%)	0.65 [0.20; 2.16]	0.486	0.65 [0.20; 2.16]	0.486

during which adjuvant chemotherapy evolved. However, to study the impact of this change, the variable of type of chemotherapy, before and after 2004, was included in the uni- and multivariate analyses. The two periods of adjuvant treatment were not found to have an influence on recurrence rates. Other limitations of the study are related to the fact that the study includes a heterogeneous patient population. However, all the patients were treated with curative intent and both univariate and multivariate analyses of several factors were performed to reduce the possible bias due to this heterogeneity and to control its impact on the endpoints. In addition, to provide specific information according to the type of complications, patients were separated into two groups: patients with perforated and patients with obstructing cancers.

Postoperative complications after colorectal cancer surgery are potential reasons for the delay or contraindication of administration of adjuvant chemotherapy. In the present study, the postoperative severe complication rate (Clavien–Dindo III–V) was 35.6%. An ASA class \geq III and blood transfusion were the only factors independently associated with severe complications.

Rates of anastomotic dehiscence were high compared to other studies [13, 14]. However, the rate fell significantly when operations were performed by a colorectal surgeon. These findings corroborate previously published results [10] and also those presented by Smith et al. in 2003, who found that specialization in colorectal surgery reduces the rate of anastomotic dehiscence and mortality after colorectal emergencies [15]. In the multivariate analysis, other factors that independently influenced anastomotic dehiscence were male gender, T4 tumor stage and blood transfusion.

Since emergency colectomies are associated with high morbidity and mortality rates, there is controversy about whether it is justified to perform a primary anastomosis in this scenario or not. In our opinion, the role of surgical specialization and a strict selection of patients for primary anastomosis may influence short- and long-term results after a curative operation. However, frequently, postoperative morbidity and mortality may to some extent be inevitable consequences of the advanced nature of the cancer and occur regardless of the surgical procedure performed.

In reference to the surgical approach performed, differences have been observed between obstructing and perforated cancers. Hartmann's procedure was more frequently performed in patients with perforated tumors. The different type of approach did not influence the postoperative complication rate.

In the present study, the postoperative mortality rate was 13.5%. It was similar to that in a recent Danish study, which reported 16% mortality in a series of 6147 patients [16].

Table 9 Univariate and multivariate analyses of prognostic variables for overall survival

	Obstruction Event N = 128/273		Univariate		Multivariate		Perforation Event N = 32/67		Univariate		Multivariate		
			HR	CI 95%	p ratio	HR	CI 95%	HR	CI 95%	p ratio	HR	CI 95%	p ratio
Gender													
Female	39 (37.9%)	Ref.	Ref.	Ref.	Ref.	Ref.	10 (40.0%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Male	89 (52.4%)	1.57 [1.08; 2.29]	0.018	1.70 (1.15; 2.51)	0.008	1.56 [0.73; 3.31]	22 (52.4%)	1.07 [1.04; 1.11]	1.07 [1.04; 1.11]	0.248	1.07 [1.04; 1.11]	1.07 [1.04; 1.11]	< 0.001
Age (SD)	71.1 (11.5)	1.04 [1.02; 1.06]	< 0.001	1.03 (1.01; 1.05)	< 0.001		71.5 (10.1)			< 0.001			< 0.001
ASA score													
I–II	65 (40.9%)	Ref.	Ref.	Ref.	Ref.	Ref.	14 (38.9%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
III	53 (54.6%)	2.12 [1.46; 3.08]	< 0.001	1.40 (0.93; 2.12)	0.105	1.67 [0.81; 3.44]	16 (57.1%)	1.01 [0.50; 2.07]	1.01 [0.50; 2.07]	0.971	1.01 [0.50; 2.07]	1.01 [0.50; 2.07]	0.971
IV	10 (58.8%)	2.46 [1.26; 4.81]	0.008	2.04 (1.01; 4.09)	0.046	1.79 [0.41; 7.91]	2 (66.7%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Site of tumor													
Proximal	63 (53.8%)	Ref.	Ref.	Ref.	Ref.	Ref.	12 (44.4%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Distal	65 (41.7%)	0.72 [0.51; 1.03]	0.070				20 (50.0%)	0.81 [0.39; 1.69]	0.81 [0.39; 1.69]	0.577	0.81 [0.39; 1.69]	0.81 [0.39; 1.69]	0.577
Peritonitis													
No	109 (46.4%)	Ref.	Ref.	Ref.	Ref.	Ref.	17 (42.5%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Localized	10 (41.7%)	0.99 [0.52; 1.91]	0.988				15 (55.6%)	1.06 [0.51; 2.20]	1.06 [0.51; 2.20]	0.880	1.06 [0.51; 2.20]	1.06 [0.51; 2.20]	0.880
Diffuse	9 (64.3%)	2.26 [1.14; 4.48]	0.020				12 (40.0%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Factor surgeon													
CS	64 (47.1%)	Ref.	Ref.	Ref.	Ref.	Ref.	20 (54.1%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
GS	64 (46.7%)	0.88 [0.62; 1.25]	0.489				13 (41.9%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
pT													
pT1–2–3	80 (49.1%)	Ref.	Ref.	Ref.	Ref.	Ref.	19 (52.8%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
pT4	47 (43.5%)	1.12 [0.78; 1.61]	0.547				18 (46.2%)	1.21 [0.60; 2.43]	1.21 [0.60; 2.43]	0.600	1.21 [0.60; 2.43]	1.21 [0.60; 2.43]	0.600
pN													
pN0	61 (46.2%)	Ref.	Ref.	Ref.	Ref.	Ref.	23 (51.1%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
pN1–2	66 (47.5%)	1.23 [0.87; 1.74]	0.245				9 (40.9%)	0.70 [0.32; 1.51]	0.70 [0.32; 1.51]	0.361	0.70 [0.32; 1.51]	0.70 [0.32; 1.51]	0.361
Lymphatic invasion													
No	73 (43.7%)	Ref.	Ref.	Ref.	Ref.	Ref.	24 (44.4%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	55 (51.9%)	1.43 [1.00; 2.03]	0.047				8 (61.5%)	1.35 [0.60; 3.03]	1.35 [0.60; 3.03]	0.462	1.35 [0.60; 3.03]	1.35 [0.60; 3.03]	0.462
Vascular invasion													
No	81 (42.4%)	Ref.	Ref.	Ref.	Ref.	Ref.	28 (46.7%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	47 (57.3%)	1.86 [1.29; 2.69]	0.001	2.05 (1.41; 2.99)	< 0.001		4 (57.1%)	1.49 [0.52; 4.29]	1.49 [0.52; 4.29]	0.455	1.49 [0.52; 4.29]	1.49 [0.52; 4.29]	0.455
Perineural invasion													
No	108 (46.2%)	Ref.	Ref.	Ref.	Ref.	Ref.	29 (46.8%)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	20 (51.3%)	1.56 [0.96; 2.53]	0.071				3 (60.0%)	1.03 [0.30; 3.53]	1.03 [0.30; 3.53]	0.961	1.03 [0.30; 3.53]	1.03 [0.30; 3.53]	0.961
Lymph nodes < 12													
No	110 (45.1%)	Ref.	Ref.	Ref.	Ref.	Ref.							
Yes	18 (62.1%)	1.25 [0.76; 2.06]	0.382										

Table 9 (continued)

	Obstruction Event N=128/273	Univariate		Multivariate		Perforation Event N=32/67	Univariate		Multivariate	
		HR	CI 95%	p ratio	HR		CI 95%	HR	CI 95%	p ratio
Chemotherapy										
No	72 (56.7%)	Ref.	Ref.	Ref.	Ref.	16 (61.5%)	Ref.	Ref.	Ref.	Ref.
<2004	26 (41.9%)	0.42	[0.27; 0.68]	< 0.001	0.41	10 (45.5%)	0.41	[0.18; 0.92]	0.031	0.031
≥2004	30 (35.7%)	0.61	[0.40; 0.94]	0.024	0.60	6 (31.6%)	0.60	[0.23; 1.55]	0.289	0.289

Many studies report higher recurrence rates in patients who had emergency surgery for colon cancer (19–45.2% in cases of obstruction, and 41.5–56.4% in perforation) [1, 5, 17, 18]. Our results are within this range and no differences were observed between obstructing and perforated cancers in terms of local and distant recurrence. Cancer-specific survival of the present series at 3 years after curative emergency resection was 77.8%, which compares favorably with that the results reported by Crozier et al. [19], who observed cancer-specific survival rates of 62% and 83% at 3 years in the emergency and elective groups, respectively.

The most common recurrence pattern in colon cancer is hematogenous spread to the liver [17, 18, 20, 21]. Some authors observed that in cases of perforation, the incidence of local and peritoneal recurrence may be higher, hypothesizing direct spread of cancer cells to the abdominal cavity [22, 23]. This concept is not universally accepted [7]. This paper shows a pattern of recurrence similar to that described in the literature, without a higher percentage of local recurrence or recurrence in patients with perforated cancer. Nevertheless, similarly to other authors [18], we found that, when diffuse peritonitis was associated with complicated cancer (both perforated and obstructing), the incidence of local recurrence rate was significantly higher.

Previous studies have found that between 60 and 80% of tumor recurrence occurs within two years of surgery [24], although it has been reported that this interval may be shorter in more ‘aggressive’ tumors [21]. In our series, factors such as perforation or advanced disease did not significantly reduce the time to recurrence.

A potential risk factor for recurrence in patients with colon cancer is the lymph node harvest [25]. Some authors maintain that fewer lymph nodes are resected in an emergency procedure than in elective surgery. However, other studies report the quality of lymphadenectomy to be similar to that of elective surgery when the same oncological criteria are applied [14, 26]. In the present study, only 10% of patients had fewer than 12 resected lymph nodes and no recurrence was found in this group. In line with previous reports of the literature [14, 20–22], we found that the presence of positive lymph nodes (N1 or N2) is a strong prognostic factor for both local and distant recurrence and cancer-related survival.

Adjuvant chemotherapy has been shown to improve overall survival in patients with stage III colon cancer [27], although it seems to have little effect in patients with

Table 10 Distribution of recurrence patterns

	[ALL] N=92	Obstruction N=68	Perforation N=24	p value
Type of recurrence				0.534
Local	13 (14.1%)	8 (11.8%)	5 (20.8%)	
Distant	62 (67.4%)	47 (69.1%)	15 (62.5%)	
Local + distant	8 (8.7%)	7 (10.3%)	1 (4.2%)	
Peritoneal carcinomatosis	9 (9.8%)	6 (8.8%)	3 (12.5%)	
Type of distant localization ^a				
Liver	37 (52.9%)	26 (48.1%)	11 (68.8%)	0.244
Lung	29 (41.4%)	26 (48.1%)	3 (18.8%)	0.071
Others	15 (21.4%)	12 (22.2%)	3 (18.8%)	1.000

^aPatients with local recurrence are not included

Fig. 2 Cumulative recurrence rate according to type of recurrence pattern

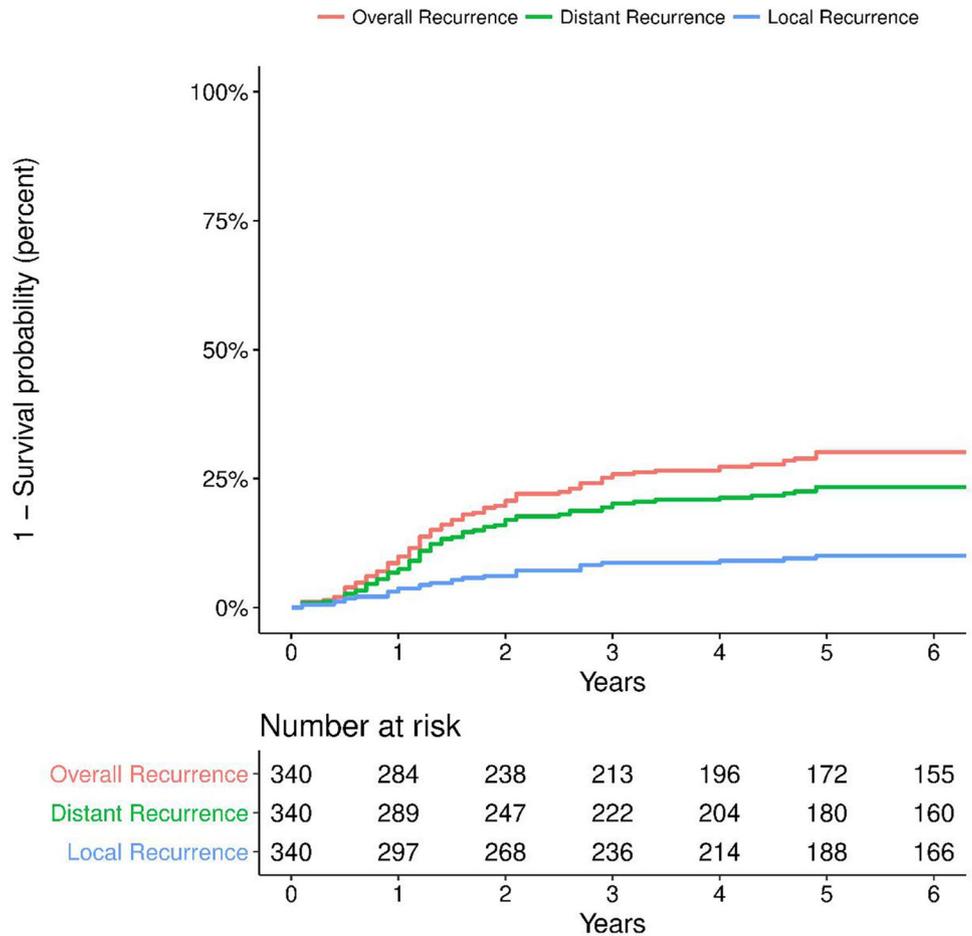


Table 11 Univariate analysis of prognostic variables for local and distant recurrence

	[ALL] N=340	Overall recurrence N=92	HR	p value	Distant recurrence N=71	HR	P value	Local recurrence N=21	HR	P value
Gender										
Female	128 (37.6%)	27 (21.1%)	Ref.	Ref.	21 (16.4%)	Ref.	Ref.	6 (4.7%)	Ref.	Ref.
Male	212 (62.4%)	65 (30.7%)	1.60 [1.02; 2.51]	0.039	50 (23.6%)	1.56 [0.94; 2.60]	0.086	15 (7.1%)	1.63 [0.63; 4.21]	0.311
Age (SD)	68.1 (11.9)	67.8 (11.8)	1.00 [0.99; 1.02]	0.716	69.0 (10.5)	1.01 [0.99; 1.03]	0.198	63.7 (15.1)	0.97 [0.94; 1.01]	0.153
ASA score										
I–II	195 (57.4%)	49 (25.1%)	Ref.	Ref.	38 (19.5%)	Ref.	Ref.	11 (5.6%)	Ref.	Ref.
III	125 (36.8%)	38 (30.4%)	1.37 [0.90; 2.09]	0.146	29 (23.2%)	1.34 [0.83; 2.18]	0.231	9 (7.2%)	1.44 [0.60; 3.49]	0.416
IV	20 (5.9%)	5 (25.0%)	1.18 [0.47; 2.97]	0.718	4 (20.0%)	1.25 [0.45; 3.50]	0.672	1 (5.0%)	1.09 [0.14; 8.45]	0.935
Site of tumor										
Proximal	144 (42.4%)	39 (27.1%)	Ref.	Ref.	30 (20.8%)	Ref.	Ref.	9 (6.3%)	Ref.	Ref.
Distal	196 (57.6%)	53 (27.0%)	1.00 [0.66; 1.51]	0.997	41 (20.9%)	0.99 [0.62; 1.59]	0.978	12 (6.1%)	0.98 [0.41; 2.32]	0.956
Initial presentation										
Obstruction	273 (80.3%)	68 (24.9%)	Ref.	Ref.	53 (19.4%)	Ref.	Ref.	15 (5.5%)	Ref.	Ref.
Perforation	67 (19.7%)	24 (35.8%)	1.39 [0.87; 2.22]	0.163	18 (26.9%)	1.32 [0.77; 2.25]	0.311	6 (9.0%)	1.54 [0.60; 3.98]	0.370
Peritonitis										
No	235 (69.1%)	55 (23.4%)	Ref.	Ref.	42 (17.9%)	Ref.	Ref.	13 (5.53%)	Ref.	Ref.
Localized	64 (18.8%)	18 (28.1%)	1.14 [0.67; 1.94]	0.631	17 (26.6%)	1.44 [0.82; 2.53]	0.203	1 (1.56%)	0.26 [0.03; 1.97]	0.191
Diffuse	41 (12.1%)	19 (46.3%)	2.16 [1.28; 3.65]	0.004	12 (29.3%)	1.70 [0.89; 3.23]	0.105	7 (17.1%)	3.30 [1.31; 8.27]	0.011
Factor surgeon										
CS	166 (48.8%)	39 (23.5%)	Ref.	Ref.	26 (15.7%)	Ref.	Ref.	13 (7.8%)	Ref.	Ref.
GS	174 (51.2%)	53 (30.5%)	1.35 [0.89; 2.04]	0.153	45 (25.9%)	1.73 [1.07; 2.80]	0.027	8 (4.6%)	0.60 [0.25; 1.44]	0.252
Anastomotic dehiscence										
No	248 (72.9%)	66 (26.6%)	Ref.	Ref.	54 (21.8%)	Ref.	Ref.	12 (4.8%)	Ref.	Ref.
No anastomosis	48 (14.1%)	14 (29.2%)	1.16 [0.65; 2.06]	0.617	10 (20.8%)	1.02 [0.52; 2.00]	0.952	4 (8.3%)	1.89 [0.61; 5.85]	0.272
Yes	44 (12.9%)	12 (27.3%)	1.08 [0.58; 2.00]	0.806	7 (15.9%)	0.73 [0.33; 1.60]	0.429	5 (11.4%)	2.49 [0.88; 7.07]	0.086
pN										
pN0	171 (50.6%)	32 (18.7%)	Ref.	Ref.	25 (14.6%)	Ref.	Ref.	7 (4.1%)	Ref.	Ref.
pN1–2	167 (49.4%)	60 (35.9%)	2.36 [1.54; 3.63]	<0.001	46 (27.5%)	2.26 [1.39; 3.69]	0.001	14 (8.4%)	2.34 [0.94; 5.80]	0.067
Lymphatic invasion										
No	212 (62.4%)	46 (21.7%)	Ref.	Ref.	38 (17.9%)	Ref.	Ref.	8 (3.8%)	Ref.	Ref.
Yes	128 (37.6%)	46 (35.9%)	1.94 [1.29; 2.92]	0.002	33 (25.8%)	1.65 [1.03; 2.63]	0.035	13 (10.2%)	3.02 [1.25; 7.29]	0.014
Vascular invasion										
No	245 (72.1%)	59 (24.1%)	Ref.	Ref.	44 (18.0%)	Ref.	Ref.	15 (6.1%)	Ref.	Ref.
Yes	95 (27.9%)	33 (34.7%)	1.67 [1.09; 2.55]	0.019	27 (28.4%)	1.83 [1.13; 2.95]	0.014	6 (6.3%)	1.12 [0.44; 2.90]	0.808
Perineural invasion										
No	294 (86.5%)	76 (25.9%)	Ref.	Ref.	58 (19.7%)	Ref.	Ref.	18 (6.1%)	Ref.	Ref.

Table 11 (continued)

	[ALL] N=340	Overall recurrence N=92	HR	p value	Distant recurrence N=71	HR	P value	Local recurrence N=21	HR	P value
Yes	46 (13.5%)	16 (34.8%)	1.59 [0.93; 2.72]	0.093	13 (28.3%)	1.70 [0.93; 3.11]	0.084	3 (6.5%)	1.18 [0.35; 4.01]	0.791
Lymph nodes < 12										
No	306 (90.0%)	82 (26.8%)	Ref.	Ref.	63 (20.6%)	Ref.	Ref.	19 (6.2%)	Ref.	Ref.
Yes	34 (10.0%)	10 (29.4%)	1.16 [0.60; 2.23]	0.667	8 (23.5%)	1.23 [0.59; 2.58]	0.575	2 (5.9%)	0.96 [0.22; 4.12]	0.956
Chemotherapy										
No	153 (45.0%)	36 (23.5%)	Ref.	Ref.	30 (19.6%)	Ref.	Ref.	6 (3.9%)	Ref.	Ref.
< 2004	84 (24.7%)	26 (31.0%)	1.22 [0.74; 2.03]	0.433	18 (21.4%)	0.97 [0.54; 1.75]	0.931	8 (9.5%)	2.20 [0.76; 6.34]	0.145
≥ 2004	103 (30.3%)	30 (29.1%)	1.12 [0.69; 1.81]	0.655	23 (22.3%)	1.03 [0.60; 1.78]	0.912	7 (6.8%)	1.53 [0.51; 4.55]	0.445

stage II cancer [28, 29]. In a study that included patients with colon cancer undergoing either elective or emergency surgery, Manfredi et al. [20] found that chemotherapy was associated with a low risk of distant recurrence in patients with stage III, and had no effect on local recurrence. Our study did not find any beneficial effect of chemotherapy on local or distant recurrence. The fact that only about 50% of the patients underwent chemotherapy may have influenced our results.

Several studies evaluated the role of colorectal specialization in elective surgery for colorectal cancer, observing a relationship with improved cancer survival [6, 15, 30–32]. However, the impact of colorectal specialization has not been previously studied in the context of patients with complicated colon cancer needing an emergency operation. In the present study, surgeons that performed the operations were divided into two groups according to their dedication to colorectal surgery or any another surgical sub-specialization of the department. The results showed that the distant recurrence rate was higher in patients operated on by general surgeons. This fact could be related to the different rate of anastomotic dehiscence which could play an important role on recurrence rates [33, 34].

The relationship between postoperative peritoneal infection and tumor recurrence has been studied in colorectal cancer and it is still an object of controversy. Goto et al. [35] evaluated the association between anastomotic dehiscence and recurrence in a series of 4919 patients. They observed a significant association with local but not distant recurrence. In contrast, Krarup et al. [36] reported that anastomotic dehiscence was associated with an increased distant recurrence rate. In our study, patients operated on by GS had a significantly higher anastomotic dehiscence rate with a higher local recurrence rate than patients operated on by CS.

Conclusions

Our study showed that male gender, diffuse peritonitis, presence of affected lymph nodes, type of surgeon and postoperative anastomotic dehiscence significantly influence cancer recurrence. No differences were observed between obstruction and perforation in terms of recurrence. In the light of these results, and since tumor biology cannot be modified, specific colorectal competency is necessary in the management of complicated colon cancer to improve results.

Table 12 Multivariate Cox-proportional regression analysis of independent prognostic variables for local and distant recurrence

	Overall recurrence		Distant recurrence		Local recurrence	
	HR	CI 95%	<i>p</i> value	HR	CI 95%	<i>p</i> value
Gender						
Female	Ref.			Ref.		
Male	1.83	(1.16; 2.88)	0.010	1.77	(1.06; 2.97)	0.030
Peritonitis						
No peritonitis	Ref.			Ref.		Ref.
Localized	1.20	(0.70; 2.05)	0.503	1.55	(0.88; 2.73)	0.132
Diffuse	2.67	(1.56; 4.56)	< 0.001	1.93	(1.00; 3.72)	0.049
Factor surgeon						
CS				Ref.		
GS				1.74	(1.07; 2.84)	0.025
Anastomotic leak						
No leak						Ref.
No anastomosis						1.23
Yes leak						(0.37; 4.16)
						0.734
pN						3.44
pN0	Ref.			Ref.		(1.15; 10.31)
pN1–2	2.48	(1.58; 3.89)	< 0.001	2.24	(1.34; 3.73)	0.002
Vascular invasion						2.74
No	Ref.			Ref.		(1.08; 6.96)
Yes	1.42	(0.91; 2.21)	0.124	1.59	(0.97; 2.62)	0.067
						0.033

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Compliance with ethical standards

Conflict of interest The authors certify that they have no competing interests.

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