DOI:10.31557/APJCC.2025.10.3.749

RESEARCH ARTICLE

Clinicopathological features of Complicated Colorectal Cancers: A 10 Year Retrospective Study in Egypt

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Abstract

Purpose: The prognosis for emergency surgery for colorectal cancers (CRCs) and metastatic tumors was reported to be extremely poor. Our objective is to ascertain the clinical characteristics of patients who have been diagnosed with complications and metastases at two tertiary centers in Egypt. **Methods:** a comparative retrospective study between complicated and non-complicated CRCs conducted in two tertiary centers in Egypt over 10 years. **Results:** a total of 320 patients underwent surgery for CRC, of which 25% underwent emergency surgery (80 cases) and 240 (75%) patients underwent an elective one. There was a higher rate of complicated colon and non-complicated rectal cancer (P=0.009). There was a significantly higher rate of positive L.Ns, positive LVI and PNI (P = 0.001), (P <0.001) and (P <0.001) respectively in complicated group. In multivariate analysis, only the tumor site (right colon P= 0.010, left colon P= 0.022) as well as the LVI (P= 0.038) remained the most important predicting factors for complication. There was a significantly higher rate of OS in patients with T1 and T2 (P= 0.002), in patients with grade I and II (P= 0.005), node-negative and non-metastatic disease with (P=<0.001) and (P= <0.001) respectively. **Conclusion:** Right and left colon cancers, along with positive LVI, are regarded as risk factors for emergency complications and metastases meanwhile advanced stages, unfavorable grades, and node-positive tumors, are associated with a poor prognosis in both groups.

Keywords: CRC- complications- emergency- metastases

Asian Pac J Cancer Care, **10 (3)**, 749-757 Submission Date: 05/16/2025 Acceptance Date: 07/01/2025

Introduction

Colorectal cancer (CRC) has emerged in recent years as the third most frequently diagnosed malignancy globally, and the second leading cause of cancer-related mortality in the United States [1, 2]. In Egypt, CRCs represented 6.5% of all reported malignant tumors. Data from the National Cancer Institute registry at Cairo University indicates that CRC ranked as the sixth most commonly documented cancer during the period of 2002–2003 [3, 4].

Large bowel obstruction occurs in approximately 15–30% of colorectal cancer (CRC) cases, while intestinal perforation is observed in only 1–10% of patients. The sigmoid colon is most frequently affected by obstruction [5]. For right-sided obstructing colon cancer, emergency surgery involving primary resection with anastomosis is widely accepted as the standard intervention. In contrast, the treatment of left-sided obstruction remains a subject of ongoing debate, with available strategies ranging from single-stage to multi-stage surgical procedures [6,7].

Maintaining quality of life requires preserving bowel function and preventing recurrence through effective treatment. Emergency surgery for complicated CRCs has a significantly worse prognosis than elective procedures,

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with a 5-year survival rate of 12–31% in obstructive cases and a high recurrence rate in cases of perforation [8, 9].

Metastatic disease continues to be the primary driver of mortality in colorectal cancer (CRC). The liver is the most frequently affected organ, accounting for 35–55% of cases, followed by the peritoneum in 1–15% of synchronous and 20–50% of metachronous metastases [10, 11]. Moreover, individuals with hepatic and/or peritoneal involvement typically face a less favorable prognosis compared to those without metastatic spread [12].

This study sought to characterize the clinical presentations of patients, alongside the pathological features of tumors, that manifested with emergency complications and metastatic spread at two tertiary centers in Egypt.

Materials and Methods

Study design

This retrospective comparative study encompassed patients who underwent emergency surgical intervention for complicated colorectal cancers (CRCs), irrespective of metastatic status, and compared them with those managed through elective surgery. The research was conducted within the Colorectal Surgery Unit at the Department of Surgery, Assiut University. Postoperative data were retrospectively reviewed from the Medical Oncology and Clinical Oncology Departments at both the Main University Hospital and the South Egypt Cancer Institute, covering the period from 2013 to 2023. The study received approval from the Institutional Review Board of Assiut University Hospital (IRB: 04-2024-300345).

The study included all colorectal cancer (CRC) patients aged over 18 years who underwent surgery during the study period. Patients with familial cancer syndromes such as hereditary nonpolyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP) as well as those with CRC arising from underlying inflammatory bowel disease (IBD), were excluded.

A comprehensive analysis of prognostic indicators in complicated colorectal cancers (CRCs) was conducted, encompassing a spectrum of epidemiological, clinical, and tumor-specific variables. Evaluated parameters included patient demographics such as age and sex, underlying comorbidities, and preoperative assessments informed by tumor location. Metastatic involvement, specifically hepatic and peritoneal spread was also considered. Additionally, tumor pathology was assessed through metrics such as stage, histologic grade, lymph vascular invasion, and perineural invasion (PNI).

For comparison, patients were categorized into two main groups: the complicated group, which included CRC cases presenting with obstruction or perforation regardless of metastatic status, and the non-complicated group, which included patients who underwent elective surgery without metastases or with metastases detected intraoperatively.

The diagnosis of obstructed and perforated CRCs was based on preoperative imaging and postoperative histopathological findings. In contrast, elective CRC cases were diagnosed through a combination of preoperative imaging, diagnostic colonoscopy, and histopathological evaluation of endoscopic biopsy samples.

Definitions and interventions

Radical resection (R0) was defined as central ligation (high tie) of the tumor's vascular pedicle along with en bloc resection of the tumor and its regional lymphatic drainage. Palliative surgery referred to procedures aimed at relieving obstruction, such as creation of a stoma for decompression or performing a bypass surgery.

Emergency surgery referred to procedures performed for obstructed or perforated CRC within the first 24 hours of hospital admission. In contrast, elective surgery involved radical resection following colorectal preparation and was typically conducted within three to four days of admission.

A tumor was considered metastatic when hepatic and/or peritoneal deposits were identified either preoperatively through imaging or intraoperatively during tumor evaluation, whether in emergency or elective settings.

Tumors located proximal to the splenic flexure were classified as right-sided colorectal cancers, whereas those located distally were designated as left-sided. Surgical resections were executed either through one-stage procedures namely, primary resection with anastomosis in elective settings, or via two-stage operations and bypass techniques during emergency presentations. For right-sided tumors, right or extended right colectomy was performed. Left-sided lesions were managed with left or extended left colectomy, anterior resection, low anterior resection (with or without a diverting ileostomy), or Hartmann's procedure, depending on the clinical context.

Statistical Analysis

All statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 22; SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation (SD) or as median and range for non-normally distributed variables, and as frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons of quantitative variables were conducted using the Mann-Whitney U test due to non-normal distribution. Categorical variables were compared using the Chi-square (χ^2) test, or Fisher's exact test when expected frequencies were below 5. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and logistic regression analysis was used to identify predictors of complications. Overall survival was analyzed using the Kaplan-Meier method, with comparisons made using the log-rank test. A p-value of <0.05 was considered statistically significant.

Results

Between 2013 and 2023, a total of 320 patients underwent surgery for colorectal cancer (CRC). Of these, 283 patients (88.4%) were under the age of 65, with a median age of 45 years (range: 18–96), and a male predominance was observed. Abdominal pain was the most common presenting symptom (41.9%), followed by chronic constipation (29.7%), rectal

Table 1. Clinicopathological Characteristics of CRC Cases

Clinic-pathological characteristics	N=320	
Age (years)		
· Mean ± SD	46.10 ± 14.23	
· Median (range)	45 (18 – 96)	
· < 65 years	283	(88.4)
· ≥ 65 years	37	(11.6)
Sex		
· Male	165	(51.6)
· Female	155	(48.4)
Clinical presentation		
· Abdominal pain	134	(41.9)
· Constipation	95	(29.7)
· Bleeding per rectum	95	(29.7)
· Intestinal obstruction	40	(12.5)
· Changing bowel habit	10	(3.1)
· Diarrhea	10	(3.1)
· Vomiting	13	(4.1)
· Others		
§ Accidentally discovered	1	(0.3)
§ Recurrent anorectal carcinoma	1	(0.3)
§ Recurrent cancer colon	14	(4.4)
§ Abdominal wall mass	1	(0.3)
§ Recurrent sigmoid cancer	1	(0.3)
§ Weight loss	7	(2.2)
§ Low back pain	1	(0.3)
Pathology		
· Adenocarcinoma	257	(80.8)
· Mucin adenocarcinoma	48	(15.1)
· Signet ring adenocarcinoma	10	(3.1)
· Squamous cell carcinoma	3	(0.9)
Tumor grade		
· Well-differentiated	48	(15.1)
· Moderate differentiated	223	(70.1)
· Poorly differentiated	44	(13.8)
· Undifferentiated	3	(0.9)
Tumor site		
· Right colon	70	(21.9)
· Left colon	73	(22.8)
· Rectum	177	(55.3)
T stage		
· T2	47	(14.7)
·T3	199	(62.2)
· T4	73	(22.8)
· Tx	1	(0.3)
N stage		
· N0	91	(28.4)
· N1	122	(38.1)
· N2	92	(28.7)
· N3	12	(3.8)
· Nx	3	(0.9)
M stage		
· M0	208	(65.0)
· M1	112	(35.0)
Received radiotherapy	143	(45.0)
K-Ras		
· Wild	56	(28.0)
· Mutant	15	(7.5.0)
· Not needed or not available	129	(64.5)
Emergency		
· No emergency	240	(75.0)
· Emergency	80	(25.0)

Quantitative data are presented as mean ± SD or median (range), and qualitative data are presented as number (percentage).

bleeding (29.7%), and intestinal obstruction (12.5%). Other less common presentations, along with detailed clinicopathological characteristics, are summarized in Table 1. Adenocarcinoma was the predominant histological type, reported in 80.8% of cases, while squamous cell carcinoma was identified in only 3 cases (0.9%). Tumor site, grade, and TNM stage are also detailed in Table 1.

Regarding surgical interventions, 80 patients (25%) underwent emergency surgery, while elective procedures were performed in 240 patients (75%). Additionally, neoadjuvant radiotherapy was administered to 143 patients (45%) of the total cohort. A summary of all demographic and clinical characteristics of the studied cases is presented in Table 1.

Table 2, the clinicopathological characteristics of complicated and non-complicated colorectal cancer (CRC) cases were analyzed. No significant differences were observed between the two groups in terms of age, sex, tumor grade, tumor stage, or K-ras mutation status. However, a significantly higher rate of complicated cases was noted in colon cancers 27.2% in right-sided and 26.5% in left-sided tumors while non-complicated cases were more frequently associated with rectal cancer (63.3%) (P=0.009). In addition, complicated cases demonstrated significantly higher rates of positive harvested lymph nodes (80.1%), lymph vascular invasion (LVI) (63.7%), and perineural invasion (PNI) (58.1%) following surgery, with statistically significant p-values $P = 0.001$, $P < 0.001$ and $P < 0.001$ respectively.

Table 3 presents the characteristics of the studied groups based on their surgical management. A significantly higher proportion of patients who underwent emergency surgery were under 65 years of age (96.3%) compared to those who had elective surgery (85.8%) ($P = 0.012$). Regarding sex distribution, a higher percentage of males underwent emergency surgery (58.8%), whereas females predominated in the elective surgery group (50.8%); however, this difference was not statistically significant.

Regarding clinical presentation, patients who underwent elective surgery were significantly more likely to present with abdominal pain ($P < 0.001$), constipation ($P < 0.001$), and vomiting ($P=0.044$) compared to those who required emergency intervention. Conversely, intestinal obstruction was the most common

Table 2. Comparison between Clinicopathological Characteristics of Complicated and Non-complicated Colorectal Cancer Cases

Clinicopathological characteristics	Non-complicated (n=169)		Complicated (n=151)		P value
Age (years)					0.739
· Mean ± SD	45.85 ± 13.96		46.38 ± 14.58		
· Median (range)	45 (18 – 96)		46 (19 – 90)		
· < 65 years	147	(87.0)	136	(90.1)	0.389
· ≥ 65 years	22	(13.0)	15	(9.9)	
Sex					0.387
· Male	91	(53.8)	74	(49.0)	
· Female	78	(46.2)	77	(51.0)	
Tumor grade					0.244
· Well to moderate differentiated	146	(87.4)	125	(82.8)	
· Poorly differentiated and undifferentiated	21	(12.6)	26	(17.2)	
Tumor site					0.009
· Right colon	29	(17.2)	41	(27.2)	
· Left colon	33	(19.5)	40	(26.5)	
· Rectum	107	(63.3)	70	(46.4)	
T stage					0.315
· Early (T2)	28	(16.6)	19	(12.6)	
· Advanced (T3+T4+Tx)	141	(83.4)	132	(87.4)	
N stage					0.001
· Negative (N0)	61	(36.1)	30	(19.9)	
· Positive (N1, N2, N3, Nx)	108	(63.9)	121	(80.1)	
Lymphovascular invasion (LVI)	45	(30.2)	79	(63.7)	<0.001
Perineural invasion (PNI)	39	(26.2)	72	(58.1)	<0.001
K-Ras*					0.5
· Wild	13	(86.7)	43	(76.8)	
· Mutant	2	(13.3)	13	(23.2)	

* The remaining cases don't have K-Ras evaluation. Quantitative data are presented as mean ± SD or median (range), qualitative data are presented as number (percentage). Significance defined by $p < 0.05$.

and significant complication necessitating emergency surgery ($P < 0.001$).

Regarding pathological characteristics, 74 patients (92.5%) who underwent emergency surgery had tumors of grade I–II, while unfavorable tumor grades were identified in only 41 patients (17.2%) and 6 patients (7.5%) in the elective and emergency groups, respectively, with a statistically significant difference ($P = 0.036$). No significant differences were observed between the two groups in terms of tumor site, K-RAS mutation status, T stage, or N stage. However, a significantly higher proportion of patients who underwent elective surgery were non-metastatic (57.5%), whereas 10 patients (12.5%) in the emergency group presented with metastases ($P < 0.001$). Additionally, lymph vascular invasion and perineural invasion were significantly more frequent among patients who underwent elective surgery ($P = 0.003$ and $P = 0.001$, respectively), as shown in table 3.

Univariate analysis revealed a significant association between complicated and non-complicated cases with respect to tumor site ($P = 0.009$), with higher complication rates observed in right-sided (27.2%) and left-sided (26.5%) colon cancers. Other significant factors included nodal stage ($P = 0.001$), lymph vascular invasion (LVI), and perineural invasion (PNI) ($P < 0.001$). However, multivariate logistic regression analysis identified tumor site specifically right colon ($P = 0.010$) and left colon ($P = 0.022$) and LVI ($P = 0.038$) as the most significant independent predictors of complications, as presented in Table 4.

The five-year overall survival (OS) based on the clinicopathological characteristics of the studied cases was assessed using Kaplan–Meier survival curves and the log-rank test. A significantly higher OS was observed in patients with early tumor stages (T1–T2) ($P = 0.002$), lower tumor grades (Grade I–II) ($P = 0.005$), node-negative status ($P < 0.001$), and non-metastatic disease ($P < 0.001$). Additionally, higher OS rates were seen in patients who underwent emergency surgery, had negative lymph vascular invasion (LVI) and perineural invasion (PNI), and received radiotherapy, all with statistically significant differences, as illustrated in Figure 1 (A–H).

Table 3. Comparison between Clinicopathological Characteristics of the Studied Colorectal Cancers According to their Management

Clinic-pathological characteristics	Elective (n=240)		Emergency (n=80)		P value
Age (years)					0.325
· Mean ± SD	46.52 ± 15.04		44.83 ± 11.46		
· Median (range)	45 (18 – 96)		45 (19 – 85)		
· < 65 years	206	(85.8)	77	(96.3)	0.012
· ≥ 65 years	34	(14.2)	3	(3.8)	
Sex					0.137
· Male	118	(49.2)	47	(58.8)	
· Female	122	(50.8)	33	(41.3)	
Clinical presentation					
· Abdominal pain	118	(49.2)	16	(20)	<0.001
· Constipation	92	(38.3)	3	(3.8)	<0.001
· Bleeding per rectum	71	(29.6)	24	(30.0)	0.944
· Intestinal obstruction	18	(7.5)	22	(27.5)	<0.001
· Changing bowel habit	10	(4.2)	0	0	0.072
· Diarrhea	8	(3.3)	2	(2.5)	1
· Vomiting	13	(5.4)	0	0	0.044
Tumor grade					0.036
· Well to moderate differentiated	197	(82.8)	74	(92.5)	
· Poorly differentiated and undifferentiated	41	(17.2)	6	(7.5)	
Tumor site					0.821
· Right colon	52	(21.7)	18	(22.5)	
· Left colon	53	(22.1)	20	(25.0)	
· Rectum	135	(56.3)	42	(52.5)	
T stage					0.927
· Early (T2)	35	(14.6)	12	(15.0)	
· Advanced (T3+T4+Tx)	205	(85.4)	68	(85.0)	
N stage					0.52
· Negative (N0)	66	(27.5)	25	(31.3)	
· Positive (N1, N2, N3, Nx)	174	(72.5)	55	(68.8)	
M stage					<0.001
· M0	138	(57.5)	70	(87.5)	
· M1	102	(42.5)	10	(12.5)	
Lymphovascular invasion (LVI)	100	(51.0)	24	(31.2)	0.003
Perineural invasion (PNI)	92	(46.9)	19	(24.7)	0.001
K-Ras*					0.194
· Wild	54	(30.5)	2	(8.7)	
· Mutant	13	(7.3)	2	(8.7)	

* The remaining cases don't have K-Ras evaluation. Quantitative data are presented as mean ± SD or median (range), qualitative data are presented as number (percentage). Significance defined by $p < 0.05$

Discussion

Despite significant advancements in colorectal cancer (CRC) treatment over the past decade, long-term survival remains poor for patients who present with emergency complications. This unfavorable prognosis is primarily attributed to high rates of recurrence and metastasis. Although approximately half of these patients undergo curative resection, postoperative morbidity and mortality are notably higher compared to elective cases. Even among those who receive curative surgery, the 5-year survival rate seldom exceeds 30% [13]. Metastatic disease is diagnosed in around 20% of CRC patients at initial presentation, and nearly half of those with localized tumors eventually develop distant spread via lymphatic, hematogenous, or peritoneal routes. Common sites of metastasis include the lymph nodes, liver, lungs, and peritoneum. While innovations in surgical techniques and systemic therapies have led to improved clinical outcomes, metastatic CRC remains predominantly incurable [14].

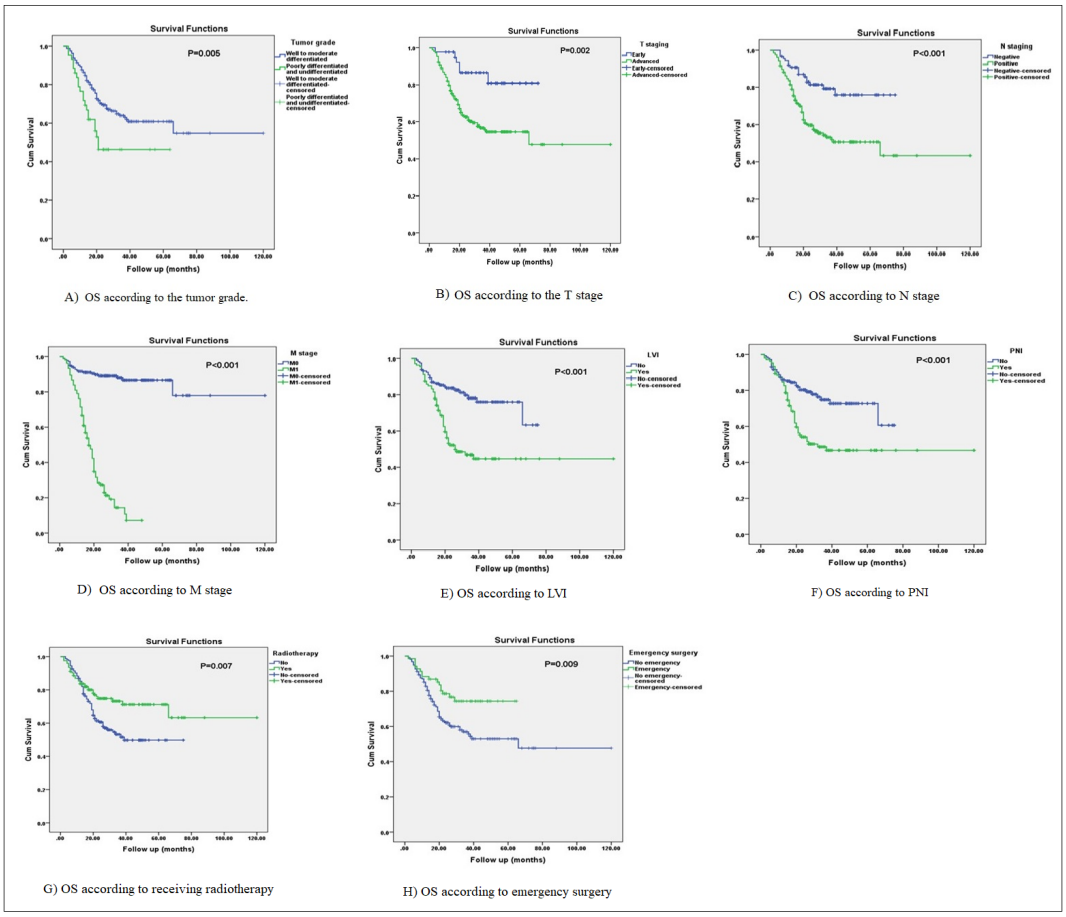

Figure 1. Kaplan Meier Curves Showing the Overall Survival (OS) According to the Clinicopathological Details of the Studied Cases. A) OS according to the tumor grade. B) OS according to T stage. C) OS according to N stage. D) OS according to M stage. E) OS according to LVI. F) OS according to PNI. G) OS according to receiving radiotherapy. H) OS according to emergency surgery

This study aimed to evaluate the risk factors associated with complications and metastases in colorectal cancer, as well as their impact on patient prognosis.

In our study, 47% of patients presented with a complication related to colorectal cancer, which is consistent with the findings of Savu et al. [15]. This high rate may be attributed to the absence of a structured CRC screening program in our region.

In this study, we observed a significantly higher rate of complications in right- and left-sided colon cancers, in contrast to a higher prevalence of non-complicated cases among rectal and rectosigmoid tumors. This finding aligns with recent epidemiological studies suggesting a potential shift in the anatomical distribution of colorectal cancer from the left to the right colon [16].

Lymph node involvement and peripheral blood lymphocyte count are important prognostic factors influencing both overall survival (OS) and disease-free survival (DFS) in colorectal cancer. Patients diagnosed at an early stage have a 5-year survival rate exceeding 75%, while those with stage III or IV disease have a markedly lower survival rate ranging between 30% and 60% [17, 18]. In our series, a higher prevalence of positive lymph node involvement was observed in the complicated group compared to the non-complicated group. This finding is consistent with previous studies [19,20], which similarly reported a greater rate of lymph node infiltration in patients with complicated CRC.

Lymph vascular invasion (LVI) and perineural invasion (PNI) are well-established poor prognostic factors in various malignancies, including colorectal cancer (CRC) [21]. In our study, both LVI and PNI were significantly more frequent in complicated cases compared to non-complicated ones. This observation is in line with the findings of Wanis et al. [22], who reported a strong association between CRC complications and the presence of LVI and PNI.

Regarding surgical intervention, 80 out of 320 patients underwent emergency surgery, while symptoms such as abdominal pain, constipation, and vomiting were more frequently associated with the elective surgery group findings that are consistent with previous studies [23, 24]. Conversely, patients who required emergency surgery are more commonly presented with intestinal obstruction, which is also well-documented in the literature [5].

The rectosigmoid junction is the most common site of colorectal cancer, followed by the left and right colon. In our series, no significant association was found between tumor location and mode of presentation. This finding may reflect the emerging trend of increasing tumor frequency in the proximal colon, as reported by Rozen et al., [25].

Pruitt et al. [26] reported an inverse relationship between

Table 4. Multivariate Logistic Regression Analysis for Prediction of Complicated CRC

			Multivariate analysis		
Variables	B	SE	OR	95% CI	P value
Tumor site					
· Right colon	0.842	0.328	2.32	1.219 – 4.415	0.01
· Left colon	0.738	0.322	2.091	1.113 – 3.930	0.022
· Rectum			ref		
N stage					
· Negative			ref		
· Positive	0.278	0.304	1.32	0.728 – 2.395	0.36
LVI					
· No			ref		
· Yes	0.909	0.437	2.481	1.053 – 5.844	0.038
PNI					
· No			ref		
· Yes	0.566	0.477	1.761	0.733 – 4.232	0.206

B: beta; SE: standard error; CI: Confidence interval; OR: Odds ratio.

emergency presentation and simple adenocarcinomas (83% vs. 85%), along with a slight, non-significant association with mucinous subtypes (12% vs. 11%). In contrast, our study found a higher proportion of emergency cases involving well and moderately differentiated adenocarcinomas, while poorly differentiated tumors were more common in elective surgeries. This discrepancy may be attributed to the smaller number of emergency cases in our cohort. Additionally, Golder et al. [27], in their systematic review and meta-analysis, reported a positive association between metastases, lymph vascular invasion (LVI), perineural invasion (PNI), and emergency presentation. However, our findings differed, likely due to the elective cases outnumbering emergency cases by a ratio of approximately 3:1.

The risk of emergency complications in colorectal cancer also appears to be influenced by tumor location, with left-sided colon cancers more commonly associated with obstruction, as previously reported [15, 28]. Our study supports these findings but also highlights a notable association between right-sided colon cancers and higher rates of complications, including emergency presentations and metastases. This may be attributed to two key factors: the right colon's greater tendency to metastasize to the liver, the most common site of CRC metastasis and the observed epidemiological shift in CRC incidence from the left to the right colon, as noted by Li and Gu [16]. Additionally, our findings confirmed that lymph vascular invasion (LVI) was significantly associated with complications, in line with previous literature [15].

Regarding survival, our study demonstrated significantly better 5-year overall survival in patients with early-stage, low-grade, node-negative, and non-metastatic colorectal cancer, aligning with the findings of Constantin et al., [13]. His report also highlighted improved survival in patients with negative lymph vascular invasion (LVI) and perineural invasion (PNI) who received radiotherapy, findings that are consistent with our results. Conversely, Yang et al., [29] identified emergency surgery as a negative prognostic factor in complicated CRC. However, our findings contradicted this, showing higher overall survival among patients who underwent emergency surgery. This discrepancy may be explained by the smaller number of emergency cases in our cohort and the higher proportion of metastatic disease among patients treated electively.

This study encompassed all colorectal cancer (CRC) cases admitted and surgically managed within a specialized colorectal surgery unit, with supplementary data gathered from two affiliated medical oncology departments at the same institution. Over a 10-year period, both elective and emergency surgeries were reviewed, including cases with and without metastatic disease. Nonetheless, several limitations were identified, notably the retrospective study design, a relatively limited sample size, and incomplete operative records particularly concerning postoperative morbidity and mortality. Additionally, the lack of hazard ratio analysis and insufficient data on microsatellite instability and other pertinent molecular biomarkers limit the depth and generalizability of certain findings.

In conclusion, right- and left-sided colon cancers, along with positive lymph vascular invasion (LVI), were identified as significant risk factors for emergency complications and metastases. Poor prognosis was associated with advanced tumor stage, high grade, and nodal involvement. The high proportion of complicated cases in our cohort reflects a substantial burden of advanced CRC in our region, underscoring the urgent need for a national colorectal cancer screening program. Future large-scale, multicenter studies incorporating genetic and molecular biomarkers are essential to further elucidate additional prognostic and risk factors.

Acknowledgements

No

Conflict of interest

No

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