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Clinicopathological comparison between right and left side recurrent colon cancer (local and metastasis)

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Abstract

Background: The second leading cause of death in the US is colorectal cancer, which affects both men and women equally. In 2018, the incidence of colorectal cancer in Iraq was third in females 918 (5.13%) and fifth in males 1018 (7.48%). Lower GI hemorrhage, stool changes, abdominal discomfort, weight loss, hunger changes, and weakness are CRC symptoms. Obstructive symptoms are especially concerning. Aim of this study: is to detect the influence of clinicopathological features of tumor site on recurrent of colon cancer.

Method: an analytic prospective cross-sectional study of 200 patients with recurrent colon CA who underwent surgical resection of colonic tumor, received treatment, and developed recurrence, dividing the patients into two groups by tumor site (right and left) and analyzing histopathological features and their impact on recurrence.

Results: In this study, 200 patients with CA colon were enrolled, with a mean age of 56.5 ± 11.5 years (range 25-86 years), 113 female patients and 87 male patients. Histopathological findings showed that 69% (138) had ulcerating macroscopically feature, 87.5% (175) had moderate grade, 66.5% (133) had T₃, and 57% (114) had T₄.

Conclusion: Recurrence is more common in 6th decade patients, overweight patients, ascending colon patients, ulcerating tumor and moderate differentiated patients, and N₁ and stage III patients in the TNM staging system. T₃ is the sole significant location of metastasis. Liver and lung recurrence are more likely in right side tumors, but not statistically significant.

Keywords: Colon Ca, right and left colon Ca, tumor side in colon Ca, metastatic colon Ca

Introduction

Colorectal cancer (CRC) is a significant global health concern, with nearly 1,200,000 new cases annually, accounting for approximately 10% of all cancer incidences and an estimated 609,000 deaths [1]. In 2010, the United States reported 141,570 new CRC cases and 51,370 deaths, representing about 10% of the country's cancer mortality [2]. In Iraq, CRC incidence ranked third in females (5.13%) and fifth in males (7.48%) in 2018. For unscreened individuals aged 50 or older, the prevalence of invasive CRC ranges from 0.5% to 2.0%, with a 25% to 40% chance of an adenoma of any size [3]. Although CRC incidence is decreasing in the United States and Canada, it is rising rapidly in Japan, Korea, and China [1]. Between 2002 and 2006, the age-standardized incidence rates in the United States were 59.0 per 100,000 for men and 43.6 for women [2]. The SEER program noted a significant increase in CRC among younger patients aged 20 to 49 years, particularly in the 40 to 44 age group, suggesting a need to lower the screening age by ten years [4, 5]. Genetic and environmental factors contribute to CRC risk. A family history of CRC doubles the risk if a first-degree relative is affected [6]. Obesity and high caloric intake are independent CRC risk factors, particularly in men [7]. Consuming red meat increases CRC risk, whereas vegetables and fruits offer protection [8]. Physical inactivity is linked to a higher CRC risk, especially for colon cancer [9]. The colon, from the ileocecal valve to the anus, is approximately 150 cm long and divided into five segments: cecum (with appendix) and ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The colon's vascular supply and lymphatic drainage are crucial for understanding CRC surgery [10]. CRC symptoms include lower GI bleeding, changes in bowel habits, abdominal pain, weight loss, and obstructive symptoms [11]. The AJCC/UICC TNM staging system is essential for CRC prognosis, with stage being the most significant factor [12].

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Histologic grade, total lymph node count, sentinel node analysis, blood or lymphatic vessel invasion, histologic type, and microsatellite instability are critical prognostic indicators [12, 13]. Factors such as preoperative carcinoembryonic antigen levels, obstruction, perforation, perineural invasion, tumor size and configuration, hemorrhage, primary tumor location, body mass index, diabetes mellitus, gender, smoking, and blood transfusions also influence prognosis [14, 15]. The overall 5-year survival rate for CRC is about 60%, with 30% to 40% of patients developing recurrent disease, usually as distant metastases or locoregional recurrence [16, 17]. Early detection of recurrence through periodic consultations, CEA testing, and imaging is crucial, along with surveillance colonoscopy [18]. Aim of this study: is to detect the influence of clinicopathological features of tumor site on recurrent of colon cancer.

Method

Study Design: This analytic prospective cross-sectional study was conducted at the Oncology Teaching Hospital and Babylon Center for Oncology from April 2020 to December 2020.

Inclusion criteria

1. Patients diagnosed with adenocarcinoma of the colon.
2. Cancer location ranged from the ileocecal valve to the sigmoid colon.
3. Patients aged 25 years or older.
4. Patients who completed surgery and chemotherapy, followed by regular check-ups with confirmed recurrence:
 - 114 patients by CT scan
 - 20 patients by dynamic MRI
 - 32 patients by PET scan
 - 34 patients by colonoscopy

Exclusion criteria

1. Stage IV at the time of diagnosis.
2. History of a second or more primary cancers.
3. Non-compliance with adjuvant treatment guidelines.
4. GIST tumors.

5. Neuroendocrine tumors.
6. Previous abdominal surgery.
7. Rectal tumors.

Data Collection

Data was collected from patient visits to the Oncology Teaching Hospital and Babylon Center for Oncology between April and December 2020.

Ethical Considerations

The study protocol was approved by the Iraqi Board for Medical Specializations. Legal authority was obtained to access patient data for research purposes, ensuring confidentiality and restricted access to unauthorized individuals.

Statistical Analysis

Data were analyzed using SPSS version 24. Descriptive statistics included frequencies, proportions, means, and standard deviations. Chi-square tests assessed associations between categorical variables, and Student's T-tests analyzed associations between categorical and continuous variables. A P-value ≤ 0.05 was considered statistically significant.

Results

A total of 200 patients with CA colon were enrolled in this study, the mean \pm SD age of patients was 56.5 ± 11.5 years, ranging between 25-86 years, table 1.

Table 1: Age to gender distribution of studied patients

Age	Gender		Total
	Male	Female	
<40 years	4(4.6%)	14(12.4%)	18(9%)
40-59 years	44(50.6%)	45(39.8%)	89(44.5%)
≥ 60 years	39(44.8%)	54(47.8%)	93(46.5%)
Total	87(43.5%)	113(56.5%)	200(100%)

The body mass index measurement for studied patients shown that: 62(31%) patients had normal BMI, 94 (47%) patients were overweight and 44(22%) patients were obese, Figure 1.

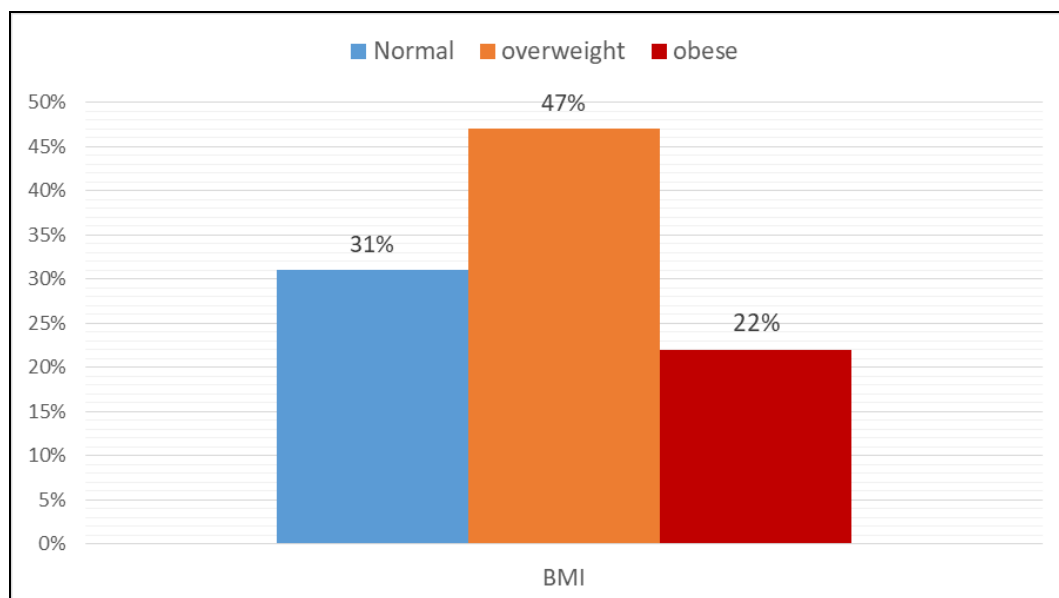


Fig 1: BMI of studied patients

The histopathological study showed that: 69%(138) of patients had ulcerating macroscopically feature, 87.5%(175) of patients had moderate grade, 66.5%(133) of patients had T3, 57%(114) of patients had 1-3 involved lymph node and 66%(132) of patients had stage III, table 2.

Table 2: Histopathological study of studied patients

Histopathological study		Number	Percentage
Macroscopic Pathological feature	Annular	3	1.5%
	Fungating	16	8%
	Polypoid	43	21.5%
	Ulcerating	138	69%
Grade	Well	16	8%
	Moderate	175	87.5%
	Poor	9	4.5%
T	T1	3	1.5%
	T2	23	11.5%
	T3	133	66.5%
	T4	41	20.5%
N	0	67	33.5%
	1-3	114	57%
	≥4	19	9.5%
Stage	I	5	2.5%
	II	63	31.5%
	III	132	66%

The side of cancer was shown in table 3. Where 126 (63%) patients had right side colonic cancer and 74 (37%) patients had left side colonic cancer.

Table 3: Side of cancer in studied patients

Side		Number	Percentage
Left	Sigmoid	55	27.5%
	Descending colon	15	7.5%
	Splenic flexure	4	2%
	Total	74	37%
Right	Cecum	20	10%
	Ascending colon	94	47%
	Hepatic flexure	12	6%
	Total	126	63%
Total		200	100%

The demographic character (age, gender and BMI) had no

association with side of colonic cancer (p>0.05), table 4.

Table 4: Relation of demographic character with side of tumor

Variables	Side		P value	
	Left	Right		
Age	<40 years	7(9.5%)	11(8.7%)	0.27*
	40-59 years	38(51.4%)	51(40.5%)	
	≥60 years	29(39.2%)	64(50.8%)	
Gender	Female	34(45.9%)	53(42.1%)	0.59*
	Male	40(54.1%)	73(57.9%)	
BMI	Normal	22(29.7%)	40(31.7%)	0.94*
	Overweight	35(47.3%)	59(46.8%)	
	Obese	17(23%)	27(21.4%)	
Total		74(100%)	126(100%)	200

*chi-square test, significant ≤0.05.

The macroscopically pathological feature, grade, lymph node status and stage had no association with side of CA colon while T status had a significant association with side of tumor (p=0.049), table 5.

Table 5: Relation of histopathological study with side of colonic cancer

Histopathological study	Side		Percentage	
	Left	Right		
Macroscopically Pathological feature	Annular	1(1.4%)	2(1.6%)	0.87*
	Fungating	5(6.8%)	11(8.7%)	
	Polypoid	18(24.3%)	25(19.8%)	
	Ulcerating	50(67.6%)	88(69.8%)	
Grade	Well	5(6.8%)	11(8.7%)	0.802*
	Moderate	65(87.8%)	110(87.3%)	
	Poor	4(5.4%)	5(5%)	
T	T1&T2	4(5.4%)	22(17.5%)	0.049*
	T3	54(73%)	79(62.7%)	
	T4	16(21.6%)	25(19.8%)	
N	N0	28(37.8%)	39(31%)	0.46*
	N1	38(51.4%)	76(60.3%)	
	N2	8(10.8%)	11(8.7%)	
Stage	I&II	28(37.8%)	40(31.7%)	0.38*
	III	46(62.2%)	86(68.3%)	
Total		74(100%)	126(100%)	200

*chi-square test, significant ≤0.05.

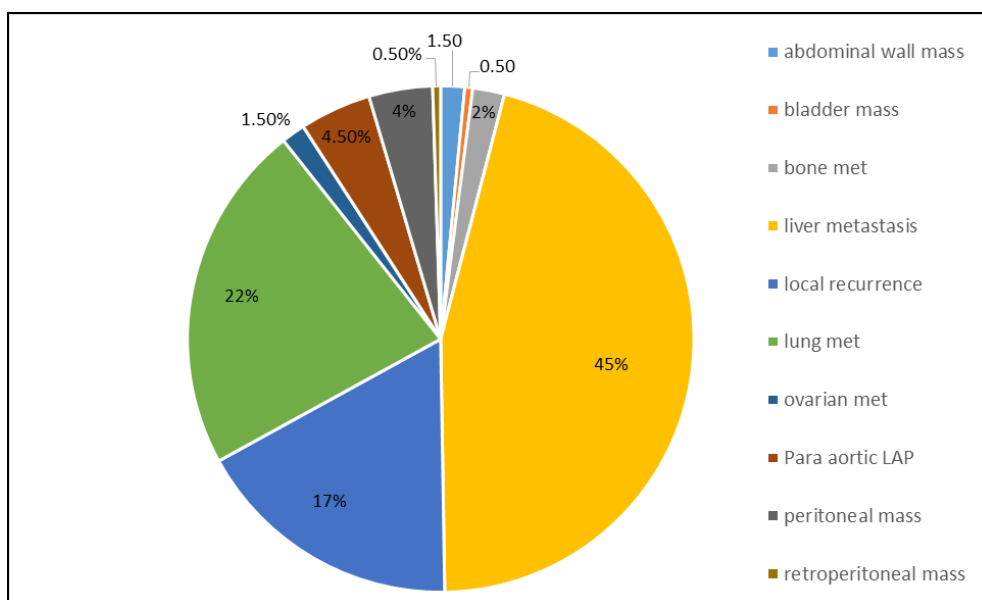


Fig 2: Site of metastasis

Relation of site of metastasis according to side of tumor was shown no significant association ($p=0.92$), in Table 6.

Table 6: Site of metastasis according to side of tumor

Metastasis	Side		Total	P value
	Left	Right		
liver metastasis	32(35.6%)	58(64.4%)	90(45%)	0.92*
local recurrence	14(41.2%)	20(58.8%)	34(17%)	
lung met	17(38.6%)	27(61.4%)	44(22%)	
Others	11(34.4%)	21(65.6%)	32(16%)	
Total	74(100%)	126(100%)	200(100%)	

*chi-square test, significant ≤ 0.05 .

Discussion

Colon cancer affects approximately 135,430 patients annually in the United States, making it the second leading cause of cancer death, with about 50,260 deaths, impacting both men and women equally [19]. While the incidence of colorectal cancer is higher in developed countries, the past decade has seen a decrease in both incidence and mortality in the United States [20]. In the current study, 200 patients with recurrent colon cancer were enrolled, aged between 25 and 86 years, with a mean age of 56.5 ± 11.5 years. Among patients with left-sided colon cancer, 7 (9.5%) were under 40 years, 38 (51.4%) were aged 40-59 years, and 29 (39.2%) were 60 years or older. For right-sided colon cancer, 11 (8.7%) were under 40 years, 51 (40.5%) were 40-59 years, and 64 (50.8%) were 60 years or older, with a P value of 0.27%, indicating no significant difference. This aligns with findings from a South Korean study by Dae Ro Lim *et al.* [21] and a Pakistani study by Mudassar Hussain *et al.*, which showed that patients with right-sided colon cancer were significantly older [22]. Gender distribution in the current study showed 87 (43.5%) females (45.9% with left-sided tumors and 42.1% with right-sided tumors) and 113 (56.5%) males (54.1% with left-sided tumors and 57.9% with right-sided tumors), with a P value of 0.59%. Similar gender distribution was reported in the South Korean study [21]. Regarding BMI, in left-sided colon cancer, 22 (29.7%) had normal BMI, 35 (47.3%) were overweight, and 17 (23%) were obese. For right-sided colon cancer, 40 (31.7%) had normal BMI, 59 (46.8%) were overweight, and 27 (21.4%) were obese. This contrasts with findings from a study in the Sulaymaniyah region, which reported higher overweight and obesity rates among left-sided tumors [23]. In terms of differentiation, the current study found 5 (6.8%) well-differentiated, 65 (87.8%) moderately differentiated, and 4 (5.4%) poorly differentiated left-sided tumors, compared to 11 (8.7%) well-differentiated, 110 (87.3%) moderately differentiated, and 5 (5%) poorly differentiated right-sided tumors, with a P value of 0.802. The South Korean study [21] reported significant differences in differentiation between left and right sides, with a P value of 0.005. Tumor size analysis in the current study showed 5 (5.4%) T1 and T2, 54 (73%) T3, and 16 (21.6%) T4 left-sided tumors, compared to 22 (17.5%) T1 and T2, 79 (62.7%) T3, and 25 (19.8%) T4 right-sided tumors, with a significant P value of 0.049. The South Korean study [21] did not find significant differences in tumor size. Lymph node involvement in the current study was 28 (37.8%) N0, 38 (51.4%) N1, and 8 (10.4%) N2 for left-sided tumors, and 39 (31%) N0, 76 (60.3%) N1, and 11 (8.7%) N2 for right-sided tumors, with a P value of 0.46. The South Korean study [21] reported significant differences

in lymph node involvement. Regarding tumor stage, the current study found 28 (37.8%) stage I and II, and 46 (62.2%) stage III left-sided tumors, compared to 40 (31.7%) stage I and II, and 86 (68.3%) stage III right-sided tumors, with a P value of 0.38. A study by Qiong Qin *et al.* [24] showed different stage distributions. Liver metastasis was found in 45% of cases, with a higher prevalence on the right side (64.4%) compared to the left (35.6%), differing from findings by Soichiro Ishihara *et al.* [25]. Lung metastasis accounted for 22% of cases, with the right side (61.4%) more affected than the left (38.6%). No significant association was found between recurrence prevalence and age, gender, BMI, grade, lymph node involvement, stage, or disease-free survival, but a significant difference was observed in tumor size (T) with a P value of 0.049. The South Korean study [21] found significant differences in lymph node involvement and grade. Significant differences in liver metastasis between right and left colon cancer were noted by Soichiro Ishihara *et al.* [25] with a P value of 0.00001.

Conclusion

There is a detective result of tumor (T) in relation to the side of the colon CA, with a more frequent recurrence on the right side of the colon. The recurrence rate is higher in patients who are obese and in the sixth decade. Recurrence is more prevalent in patients whose primary tumor is situated in the ascending colon. In terms of histopathological characteristics, ulcerating tumors and moderately differentiated tumors are more prevalent, while recurrence is more prevalent in T3, N1, and stage III according to the TNM staging system. These characteristics are more prevalent in the right side. In terms of the location of metastasis, liver recurrence is more prevalent than lung recurrence, and right-side tumors are more prevalent.

Conflict of Interest

Not available

Financial Support

Not available

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