

## Assessment of Incidence of Metachronous Neoplasms after Surgical Resection of Colorectal Cancer

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### ABSTRACT

**Background:** Colorectal cancer (CRC) is among the most common malignancies worldwide, with significant morbidity and mortality. Despite curative surgical resection, patients remain at risk of developing metachronous colorectal neoplasms.

**Aim:** This study aims to determine the incidence and risk factors of metachronous CRC following curative surgery.

**Methods:** In this retrospective cohort study, 100 patients who underwent curative CRC surgery and were followed for six months. Patients with total colectomy, metastatic CRC, or palliative surgeries were excluded. Surveillance included colonoscopy, CT imaging, and laboratory investigations. Patients were categorized into two groups: recurrence (Group 2, n = 10) and no recurrence (Group 1, n = 90).

**Results:** The incidence of metachronous CRC was 10%, equally distributed as polyps (5%) and masses (5%). Recurrence occurred most frequently at the anastomotic site (40%). Adenocarcinoma was the most common histopathology (50%). No significant differences were found between groups regarding demographic or surgical variables. However, diabetes mellitus (DM) was significantly associated with recurrence (60% in Group 2 vs. 26.7% in Group 1,  $p = 0.048$ ), and multivariate analysis confirmed DM as an independent predictor (OR = 10.619; 95% CI: 1.002–112.557;  $p = 0.049$ ). Laboratory parameters showed significant postoperative changes, especially in liver and renal function tests, but these did not independently predict recurrence.

**Conclusion:** Metachronous CRC occurred in 10% of patients within six months post-resection. Diabetes mellitus emerged as a significant independent predictor. Vigilant surveillance, especially in diabetic patients, is essential to detect early metachronous lesions.

**Keywords:** Colorectal Cancer, Metachronous Neoplasm, Diabetes Mellitus, Surgical Resection.

### INTRODUCTION

Colorectal Cancer (CRC) is the world's third most prevalent CRC with an advanced death rate. However, colorectal carcinoma is not just a single form of tumor; its pathogenesis varies from right to left sides of the colon to the position of the anatomic malignant tumor [1].

The molecular properties and histology of proximal colon (right) and distal (left) tumors are varying. In addition to their origin, these tumors show a distinct histology. While tumors of the right side show serrated sessile adenomas or mucinous adenocarcinomas, left sided tumors can present as tubular, villous or atypical adenocarcinomas. Having a polypoid morphology, left sided tumors are easier to spot early in comparison to those of the right side. [1].

In the rectum-sigmoid flexure, distal colon or left-side tumors frequently occur, and they are not always easy to distinguish from rectal tumors. A tumor is considered rectal if it occurs within 15 cm of the anal sphincter [2].

Rectal cancers have a higher rate of loco-regional relapse and lung metastases, while colon cancers have a higher incidence of hepatic

tropism for the liver and have a marginally better overall prognosis. Metachronous CRCs are tumors that grow at a different location than the primary tumor occurring six months or longer after curative surgery. Besides that, colon cancer's proximal position is a risk factor for the development of metachronous CRC [2].

Patients with CRC are susceptible to developing metachronous CRC in the remaining segment of the large intestine over time. The risk is influenced by the extent of bowel resection, with segmental versus extensive resection potentially modifying the likelihood of metachronous CRC occurrence. This is shown by individuals suffering from lynch syndrome whose metachronous CRC risk varies depending on the form of operation and the bowel length of the original colon cancer. The clinical effect of improved bowel movements and the detrimental effect on quality of life after wider surgery must be balanced against a decrease of the risk of metachronous CRC [3].

Curative surgical resection is the primary treatment strategy for non-metastatic colon cancer. The consideration of adjuvant

chemotherapy postoperatively depends on the pathological staging of the disease. Adenomatous polyps are common and should be removed because of its precancerous potential. The duration of the post-polypectomy surveillance should be assessed on the basis of the probability of metachronous neoplasm and the limited monitoring time should be recommended in high-risk classes [4].

Surveillance recommendations following polypectomy suggest that the risk of advanced metachronous neoplasms is heightened in patients with the following characteristics: (1) three or more adenomas, (2) adenomas measuring at least 10 mm, (3) high-grade dysplasia in adenomas, (4) villous histology in adenomas, or (5) serrated adenomas of 10 mm or greater. Despite these associations, a thorough evaluation of these risk factors during postoperative monitoring for advanced metachronous neoplasms has not been fully conducted [4].

This study aims to determine the incidence of metachronous neoplasms following curative surgical resection of CRC and to evaluate the various risk factors contributing to the development of metachronous colorectal cancer.

## MATERIALS AND METHODS

### Study Design and Population

A total of 100 patients who underwent curative surgical resection of CRC between 2018 and 2020 at Ain Shams University Hospitals were enrolled in this retrospective cohort study.

### Eligibility Criteria

**Inclusion Criteria:** Patients  $\geq 18$  years and patients after curative surgical resection of CRC.

**Exclusion Criteria:** Patients were excluded from the study if they had undergone total colectomy, received neoadjuvant radiotherapy or chemotherapy, or had surgery performed for palliative intent. This included palliative resection, debulking, bypass procedures, or colostomy/ileostomy for symptom relief due to obstruction, as well as cases of metastatic CRC involving other organs.

### Pre-operative assessment

**History taking:** Personal history: (name, sex, age, smoking, alcohol), presenting symptoms: bleeding per rectum, loss of weight and pallor, family history of CRC and history of inflammatory bowel disease.

**Clinical examination:** Any palpable abdominal mass by palpation and PR examination for rectal mass or bleeding.

**Colonoscopy:** Informed consent obtained. Risks of procedure, benefits and alternatives were explained and understood. Medication of anesthesia was midazolam or propofol. Taking multiple biopsies from suspected regions for histopathologically examination to detect adenocarcinoma.

**Radiological investigations:** Computed tomography (CT) finding: to detect any colon mass or mural thickening.

**Laboratory investigations:** CBC (Hb, PLT, TLC), liver functions test (AST, ALT, Total Bilirubin, Direct Bilirubin and albumin), kidney functions test (serum creatinine and serum urea).

### Operative management

Type of operation was done according to the site of the tumor: Right hemicolectomy for cecal mass and ascending colon, left hemicolectomy for descending colon, extended hemicolectomy for transverse colon and abdominal perineal resection for anorectal cancer.

### Post-operative follows up:

We included colonoscopy or computed tomography (CT) finding data and laboratory tests as follow up method to evaluate incidence of advanced Metachronous neoplasms during postoperative surveillance. All of the colonoscopy operations were carried out by colonoscopists with a lot of experience. Patients who underwent an unexpected perioperative colonoscopy were scheduled to have their first postoperative colonoscopy within six months. A colonoscopy was deemed complete if visualization and documentation of the cecal base, ileocecal valve, or terminal ileum were achieved and reported.

Anastomotic recurrence was defined as tumor development in the previous anastomotic suture line, regardless of synchronous or other local recurrence. Polyps of various sizes were removed and examined histopathologically. This preoperative colonoscopy was used to establish the absence of colonic lesions. Advanced adenoma was defined as a tubular adenoma with a diameter less than 10 mm; adenoma with villous or Tubulovillous histology; or adenoma with high-grade dysplasia. Any of these three previously identified diagnoses of advanced adenoma or CRC was considered as advanced neoplasm. In each patient, we documented all

sorts of neoplastic lesions, including those with the most advanced stage. Other non-neoplastic colorectal lesions include hyperplastic polyps and other non-neoplastic colorectal lesions. Metachronous lesions were defined as those encountered at least six months following surgery.

Patients were divided into two groups based on postoperative outcomes: Group 1, consisting of 90 patients who showed no recurrence, and Group 2, which included 10 patients who experienced recurrence.

#### **Ethics approval and consent of participation**

**The present study was done after obtaining the approval from the Ethical Committee at Ain Shams University Hospitals, and the study was conducted in accordance with the principles of the Declaration of Helsinki. All participants provided a written informed consent before enrollment. Informed consent was formally obtained from the patients after they were adequately informed.**

#### **Statistical analysis**

Data were analyzed using the IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were presented as numbers and percentages, while the Kolmogorov-Smirnov test was used to assess the normality of distribution. Quantitative data were summarized using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The significance of results was assessed at the 5% level. For categorical variables, the Chi-square test was

used to compare different groups, with Fisher's Exact or Monte Carlo correction applied when more than 20% of the cells had an expected count of less than 5. For normally distributed quantitative variables, the Student t-test was used to compare two groups, while the paired t-test was used to compare two periods. For abnormally distributed quantitative variables, the Mann-Whitney test was used to compare two groups, and the Wilcoxon signed-rank test was used for comparisons between two periods.

#### **RESULTS**

Among the recurrence cases, 5% ( $n = 5$ ) presented as polyps, and 5% ( $n = 5$ ) as masses, indicating an equal distribution of recurrence types. Recurrence was most common at the anastomosis (40.0%,  $n = 4$ ) and least in the left-side colon (10.0%,  $n = 1$ ). Adenocarcinoma was the predominant histopathology (50.0%,  $n = 5$ ), followed by Tubulovillous polyps (20.0%,  $n = 2$ ), while other polyp types each accounted for 10.0% ( $n = 1$ ).

There were no significant differences between Group 1 ( $n = 90$ ) and Group 2 ( $n = 10$ ) in sex, age, BMI, smoking, alcohol consumption, anemia, bleeding, weight loss, lesion site, or type of surgery ( $p > 0.05$ ). Diabetes mellitus was more frequent in Group 2 (60.0%) but not statistically significant ( $p = 0.066$ ). A family history of CRC was significantly higher in Group 2 (20.0%) ( $p = 0.009$ ). The most common lesion site was the left colon (47.0%), and left hemicolectomy (62.0%) was the most performed procedure, with no significant differences between groups ( $p = 0.393$ ,  $p = 0.728$ ). **Table 1**

**Table 1: Comparison between the two studied groups according to demographic data, BMI (Kg/m<sup>2</sup>), risk factors of CRC, presenting symptoms, lesion site, and type of operation.**

	Total (n= 100)	Group (1) (n = 90)	Group (2) (n = 10)	p-value
	N( %)	N( %)	N( %)	
<b>Sex</b>				
Male	64(64.0)	59(65.5)	5(50.0)	0.489
Female	36 (36.0)	31(34.4)	5(50.0)	
<b>Age (years)</b>				
Median (IQR)	50.0 (32.0 –60.0)	51.0 (31.0 – 60.0)	44.0 (38.0 – 62.0)	0.835
<b>BMI (Kg/m<sup>2</sup>)</b>				
Normal.	21(21.0)	18(20.0)	3(30.0)	MCp= 0.745
Over weight	26(26.0)	24(26.7)	2(20.0)	
Obese	53(53.0)	48(53.3)	5(50.0)	
Median (IQR)	30.50(25.0 – 33.0)	30.50(25.0 – 33.0)	31.0(24.0 – 33.0)	
<b>Alcohol</b>				
Non alcoholic	99(99.0)	89(98.9)	10(100.0)	FEp= 1.000
<b>Smoking</b>	28(28.0)	26(28.9)	2(20.0)	FEp= 0.721
<b>DM</b>	31(31.0)	25(27.8)	6(60.0)	FEp= 0.066
<b>IBD</b>				
No	92(92.0)	82(91.1)	10(100.0)	MCp= 1.000
Crohns	3(3.0)	3(3.3)	0(0.0)	
Ulcerative colitis	5(5.0)	5(5.6)	0(0.0)	
<b>Family history</b>				
No	98(98.0)	90(100.0)	8(80.0)	FEp= 0.009*
<b>Anemia</b>	79(79.0)	71(78.9)	8(80.0)	1.000
<b>Bleeding</b>	64(64.0)	59(65.6)	5(50.0)	0.489
<b>Weight loss</b>	82(82.0)	73(81.1)	9(90.0)	0.685
<b>Lesion site</b>				
Right colon	29(29.0)	26(28.9)	3(30.0)	0.393
Left colon	47(47.0)	44(48.9)	3(30.0)	
Transverse colon	5(5.0)	4(4.4)	1(10.0)	
Rectal colon	19(19.0)	16(17.8)	3(30.0)	
<b>Type of operation</b>				
Right hemicolectomy	29(29.0)	26(28.9)	3(30.0)	0.728
Left hemicolectomy	62(62.0)	56(62.2)	6(60.0)	
Extended left hemicolectomy	5(5.0)	4(4.4)	1(10.0)	
Abdominal perineal resection (APR)	4(4.0)	4(4.4)	0(0.0)	

n: Number of cases, Min. – Max. :Minimum – Maximum , Mean ± SD : Mean ± Standard Deviation , Median (IQR) : Median (Interquartile Range) , BMI (Kg/m<sup>2</sup>) : Body Mass Index (Kilograms per square meter) , MCP : Monte Carlo p-value (used in categorical data analysis) , FEP : Fisher's Exact p-value (used for small sample categorical data) , DM : Diabetes Mellitus , IBD : Inflammatory Bowel Disease , APR : Abdominal Perineal Resection, \*,\*: significant p-value <0.05.

Postoperatively, Hb increased in Group 2 (p = 0.046), while WBCs decreased (p = 0.011). PLT declined in both groups but it was not significant (p > 0.05). No other substantial differences were observed. **Table 2**

**Table 2: Comparison between the two studied groups according to CBC**

	CBC	Total (n= 100)	Group (1) (n = 90)	Group (2) (n = 10)	p-value
Hb	<b>Pre</b>				
	Mean $\pm$ SD.	8.80 $\pm$ 2.27	8.88 $\pm$ 2.31	8.13 $\pm$ 1.82	0.327
	<b>Post</b>				
	Mean $\pm$ SD.	8.92 $\pm$ 2.52	8.83 $\pm$ 2.54	9.72 $\pm$ 2.29	0.29
	<b>t<sub>1</sub>(p<sub>1</sub>)</b>	<b>0.361(0.719)</b>	<b>0.143(0.887)</b>	<b>2.317*(0.046*)</b>	
PLT	<b>Pre</b>				
	Mean $\pm$ SD.	233.27 $\pm$ 84.28	235.34 $\pm$ 86.56	214.60 $\pm$ 60.15	0.509
	<b>Post</b>				
	Mean $\pm$ SD.	209.49 $\pm$ 74.83	213.71 $\pm$ 77.17	171.50 $\pm$ 30.31	0.108
	<b>Z (p<sub>1</sub>)</b>	<b>1.821(0.069)</b>	<b>1.396(0.163)</b>	<b>1.683(0.092)</b>	
WBCs	<b>Pre</b>				
	Median (IQR)	7.80 (6.30 – 11.0)	7.85 (6.30 – 11.0)	7.35 (6.0 – 10.0)	0.465
	<b>Post</b>				
	Median (IQR)	7.25 (5.80–10.0)	7.30 (5.90–10.0)	5.70 (4.30–8.0)	0.061
	<b>Z (p<sub>1</sub>)</b>	<b>2.010*(0.044*)</b>	<b>1.447(0.140)</b>	<b>2.547*(0.011*)</b>	

CBC: Complete Blood Count, Hb: Hemoglobin, PLT: Platelets, WBCs: White Blood Cells, SD: Standard Deviation, IQR: Interquartile Range.

Postoperatively, ALT, AST, T.BIL, and D.BIL increased significantly in the total cohort and Group 1 ( $p < 0.001^*$ ), while Group 2 showed a significant T.BIL rise ( $p = 0.018^*$ ). Albumin decreased significantly in the total cohort and Group 1 ( $p < 0.001^*$ ), but not in Group 2. Preoperative ALT was higher in Group 2 ( $p = 0.032^*$ ), with no significant postoperative variations between groups. **Table 3**

**Table 3: Comparison between the two studied groups according to liver functions**

	Liver function	Total (n= 100)	Group (1) (n = 90)	Group (2) (n = 10)	value
ALT	<b>Pre</b>				
	Mean $\pm$ SD.	32.34 $\pm$ 7.61	31.88 $\pm$ 7.34	36.50 $\pm$ 9.12	.032*
	<b>Post</b>				
	Mean $\pm$ SD.	46.71 $\pm$ 7.33	47.60 $\pm$ 7.59	38.74 $\pm$ 2.92	.219
	<b>Z (p<sub>1</sub>)</b>	<b>6.145*(&lt;0.001*)</b>	<b>6.218*(&lt;0.001*)</b>	<b>0.280(0.779)</b>	
AST	<b>Pre</b>				
	Mean $\pm$ SD.	31.46 $\pm$ 6.26	31.13 $\pm$ 6.16	34.40 $\pm$ 6.69	.100
	<b>Post</b>				
	Median (IQR)	39.50 (30.0 – 62.0)	39.50 (31.0 – 67.0)	38.0 (25.0 – 57.30)	.303
	<b>Z (p<sub>1</sub>)</b>	<b>6.170*(&lt;0.001*)</b>	<b>6.163*(&lt;0.001*)</b>	<b>0.949(0.343)</b>	
Albumin	<b>Pre</b>				
	Mean $\pm$ SD.	4.13 $\pm$ 0.37	4.15 $\pm$ 0.37	3.98 $\pm$ 0.32	.156

	<b>Post</b>				
	Median (IQR)	3.70 (3.50 – 4.05)	3.70 (3.50 – 4.0)	3.75 (3.40 – 4.10)	
	<b>Z (p<sub>1</sub>)</b>	<b>5.752*(&lt;0.001*)</b>	<b>5.523*(&lt;0.001*)</b>	<b>1.611(0.107)</b>	
	<b>Pre</b>				
<b>T.BIL</b>	<b>Post</b>				
	Median (IQR)	0.63 (0.42 – 0.90)	0.63 (0.42 – 0.90)	0.62 (0.51 – 0.80)	
	<b>Z (p<sub>1</sub>)</b>	<b>7.257*(&lt;0.001*)</b>	<b>6.926*(&lt;0.001*)</b>	<b>2.366*(0.018*)</b>	
	<b>Pre</b>				
<b>D.BIL</b>	<b>Post</b>				
	Median (IQR)	0.18 (0.20 – 0.90)	0.18 (0.10 – 0.20)	0.19 (0.10 – 0.20)	
	<b>Z (p<sub>1</sub>)</b>	<b>7.643*(&lt;0.001*)</b>	<b>7.442*(&lt;0.001*)</b>	<b>1.802(0.072)</b>	
	<b>Pre</b>				

ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, T.BIL: Total Bilirubin, D.BIL: Direct Bilirubin, SD: Standard Deviation, IQR: Interquartile Range, Z: Wilcoxon Signed-Rank test statistic, \*: significant p-value <0.05.

Serum creatinine and urea significantly increased postoperatively in the total sample and Group 1 ( $P < 0.001$ ), but not in Group 2 ( $P = 0.233$ ,  $P = 0.086$ ). No notable variations were found between groups pre- and postoperatively ( $P > 0.05$ ). **Table 4**

**Table 4: Comparison between the two studied groups according to renal functions**

Comparison between the two studied groups according to renal functions						
		Renal function	Total (n= 100)	Group (1) (n = 90)	Group (2) (n = 10)	p-value
Pre						
S. CREAT	Median (IQR)	Pre				0.189
		Post	1.0 (0.80 – 1.20)	1.0 (0.80 – 1.20)	1.15 (0.90 – 1.30)	
	Median (IQR)	Pre				0.899
		Post	1.12 (0.90 – 1.43)	1.16 (0.90 – 1.45)	1.10 (0.90 – 1.40)	
Z (p <sub>1</sub> )		4.639*(<0.001*)	4.534*(<0.001*)	1.192(0.233)		
Pre						
S. UREA	Median (IQR)	Pre				0.311
		Post	30.0 (22.0 – 40.0)	30.0 (22.0 – 40.0)	35.0 (25.0 – 45.0)	
	Median (IQR)	Pre				0.814
		Post	47.0 (30.0 – 75.65)	47.0 (30.0 – 76.0)	53.50(26.0 – 75.30)	
Z (p <sub>1</sub> )		6.133*(<0.001*)	5.939*(<0.001*)	1.719(0.086)		

S. CREAT: Serum Creatinine, S. UREA: Serum Urea, Z: Wilcoxon Signed-Rank test statistic, \*: significant p-value <0.05.

Diabetes mellitus ( $p = 0.048$ , OR = 3.900, 95% CI: 1.014 – 14.993) was the only significant predictor in both univariate and multivariate analysis. Other factors, including sex, age, BMI, smoking,

anemia, bleeding, lesion site, type of operation, and biochemical markers, showed no significant associations ( $p > 0.05$ ), though ALT, AST, serum creatinine, and serum urea trended toward significance.

**Table 5**

**Table 5: Univariate and multivariate Logistic regression analysis for the parameters affecting Recurrence lesions (mass and polyps)**

	Univariate		#Multivariate	
	P	OR (95%C. I)	P	OR (95%C. I)
Sex (male)	0.377	1.903(0.512 – 7.079)		
Age (years)	0.833	1.005(0.962 – 1.050)		
BMI (Kg/m2)	0.880	0.991(0.885 – 1.110)		
Alcohol	1.000	–		
Smoking	0.556	0.615(0.122 – 3.095)		
DM	0.048*	3.900(1.014 – 14.993)	0.048*	3.900(1.014 – 14.993)
IBD	0.999	–		
Family history	0.999	–		
Anemia	0.496	2.096(0.248 – 17.678)		
Bleeding	0.337	0.525(0.141 – 1.954)		
Weight loss	0.935	1.070(0.210 – 5.464)		
Lesion site				
Rt				
Lt	0.537	0.591(0.111 – 3.1460)		
Transverse	0.544	2.167(0.179 – 26.290)		
Rectal	0.579	1.625(0.292 – 9.050)		
Type of operation				
Right hemicolectomy				
Left hemicolectomy	0.921	0.929(0.215 – 4.006)		
Extended left hemicolectomy	0.544	2.167(0.179 – 26.290)		
Abdominal perineal resection (APR)	0.999	–		
Hb pre	0.326	0.850(0.615 – 1.175)		
PLT pre	0.460	0.997(0.988 – 1.005)		
WBCs pre	0.374	0.905(0.726 – 1.128)		
ALT pre	0.078	1.113(0.988 – 1.255)		
AST pre	0.127	1.103(0.973 – 1.250)		
Albumin pre	0.179	0.262(0.037 – 1.851)		
D.BIL pre	0.604	3.381(0.034 – 335.614)		
S. CREAT pre	0.122	6.852(0.597 – 78.656)		
S. UREA pre	0.090	1.027(0.996 – 1.060)		

OR: Odds Ratio, CI: Confidence Interval, BMI: Body Mass Index, DM: Diabetes Mellitus, IBD: Inflammatory Bowel Disease, Rt: Right, Lt: Left, APR: Abdominal Perineal Resection, Hb: Hemoglobin, PLT: Platelet Count, WBCs: White Blood Cells, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, D.BIL: Direct Bilirubin, S. CREAT: Serum Creatinine, S. UREA: Serum Urea.

DM remained a significant predictor ( $P = 0.049$ ,  $OR = 10.619$ , 95% CI: 1.002 – 112.557), while family history lost significance in multivariate analysis ( $P = 0.065$ ). Other variables showed no significant associations. **Table 6**

**Table 6: Univariate and multivariate Logistic regression analysis for the parameters affecting recurrence mass**

	Univariate		#Multivariate	
	P	OR (95%C. I)	P	OR (95%C. I)
Sex (male)	0.849	1.196(0.190 – 7.514)		
Age (years)	0.848	0.994(0.936 – 1.056)		
BMI (Kg/m2)	0.590	0.958(0.820 – 1.120)		
Alcohol	1.000	–		
Smoking	0.544	1.769(0.280 – 11.198)		
DM	0.043*	10.074(1.077 – 94.270)	0.049*	10.619(1.002 – 112.557)

IBD	0.999	—		
Family history	0.036*	23.500(1.234 – 447.595)	0.065	26.963(0.818 – 889.184)
Anemia	0.998	—		
Bleeding	0.457	2.333(0.251 – 21.713)		
Weight loss	0.955	1.067(0.113 – 10.081)		
Lesion site				
Rt				
Lt	0.729	0.609(0.037 – 10.124)		
Transverse	0.198	7.0(0.362 – 135.517)		
Rectal	0.345	3.294(0.277 – 39.138)		
Type of operation				
Right hemicolectomy				
Left hemicolectomy	0.764	1.424(0.142 – 14.306)		
Extended left hemicolectomy	0.198	7.0(0.362 – 135.517)		
Abdominal perineal resection (APR)	0.999	—		

P: P-value (statistical significance level), OR: Odds Ratio, 95% C.I.: 95% Confidence Interval, BMI: Body Mass Index (Kg/m<sup>2</sup>), DM: Diabetes Mellitus, IBD: Inflammatory Bowel Disease, Hb: Hemoglobin, PLT: Platelet Count, WBCs: White Blood Cells, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, D.BIL: Direct Bilirubin, S. CREAT: Serum Creatinine, S. UREA: Serum Urea, Rt: Right, Lt: Left, APR: Abdominal Perineal Resection.

## Discussion

Cancer colon is the third most common cancer globally, with high mortality in advanced stages [5]. Its incidence and mortality have declined in the U.S. but remain significant in Egypt and the Middle East [6]. Metachronous neoplasms are variably defined, often as lesions appearing at least six months post-colectomy [7], [4]. This retrospective cohort study analyzed 100 patients who underwent curative resection at Ain Shams University Hospitals, Cairo, Egypt, between 2018 and 2020. Patients were followed up for six months using colonoscopy, CT, and lab tests to detect advanced metachronous neoplasms. The study population had a male-to-female ratio of 1.7:1.

In our study, the enrolled patients had a higher proportion of males than females, with an average middle-aged demographic.

This result aligns with Nam & Shin [4] in terms of gender distribution but differs in age.

According to the incidence of recurrent neoplasms, our study population was divided into two groups: Group 1 including patients without CRC recurrence and Group 2 including patients with recurrent CRC.

The incidence of metachronous cancer in this study was differed from Cho *et al.* [7] and Nam & Shin [4].

The incidence of metachronous polyps in this study differed from Nam & Shin [4], who reported higher recurrence rates.

Most patients in the present study were obese or overweight, with no statistically significant difference in BMI between the two groups. This could suggest the association between obesity and the incidence of CRC, but a

direct causal association between obesity and metachronous neoplasms could not be identified in our study.

Previous studies revealed that metabolic syndrome including DM and obesity were associated with colon polyps & metachronous polyps' recurrence after polypectomy where Chiu *et al.* [8] stated that patients with metabolic syndrome had a significantly higher risk for advanced neoplasms also, Nam & Shin [4] revealed obesity as a risk factor of metachronous neoplasms.

Most patients presented with anemia, bleeding, and weight loss, with no significant difference between the two groups in symptoms.

These findings differ from McCulloch *et al.* [9], who reported lower anemia and bleeding rates in younger CRC patients, increasing with age.

So, we can consider anemia, bleeding and loss of weight as red flags of CRC but in our study none of these risk factors were significantly different between both groups.

In this study, the left colon was the most common site for initial lesions, likely due to early presentation and easier detection, while recurrence was most frequent at the anastomosis site. However, there was no significant difference between the study groups regarding the initial lesion site or its impact on the recurrence.

Although left-sided CRC was the most common lesion site, it did not significantly impact the incidence of metachronous lesions, differing from previous studies that found a significant association.

In the current study, we evaluated the laboratory results of patient's pre-operative and



post-operative as follow up with complete blood count, liver function tests (Alt, Ast, Total bilirubin and Direct bilirubin) and kidney function tests (serum creatinine and blood urea).

A significant difference was observed between pre- and post-operative laboratory results, particularly in WBCs, liver function tests (ALT, AST, Albumin, T.BIL, D.BIL), and kidney function tests (s. creat and urea).

This finding aligns with **Goshen *et al.*** <sup>[10]</sup>, who also reported significant differences in pre- and post-operative laboratory results, including WBCs, ALT, AST, and Bilirubin.

A significant difference was observed between the two groups in pre-operative ALT, aligning with **Goshen *et al.*** <sup>[10]</sup>, who also reported a significant ALT value.

**Lin *et al.*** <sup>[11]</sup> identified ALT as an independent predictor for recurrent colorectal polyps, but this was not observed in our study, where ALT did not show statistical significance in recurrence.

Univariate and multivariate logistic regression analyses identified DM as a significant factor associated with metachronous CRC.

This result aligns with previous studies demonstrating a significant association between DM and increased CRC risk, though our study found no gender-related impact on recurrence.

There are some limitations to this study. First, due to the retrospective design of this study, selection bias cannot be avoided. Second, while the majority of patients had colonoscopies in compliance with the post-colectomy surveillance guidelines, some patients' follow-up intervals were irregular due to their medical conditions. Third, short follow up period of this study and small number of patients compared to other studies.

### Conclusion

Metachronous colorectal neoplasms occurred in 10% of patients within six months post-resection, with diabetes mellitus emerging as the only significant independent predictor. Enhanced surveillance is recommended for diabetic patients to enable early detection and improve outcomes.

### Declarations

### Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Data availability

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

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