

# Colorectal cancer in GIT and Baghdad teaching hospital

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## ABSTRACT

**Background:** Colorectal carcinoma (CRC) is one of the most common form of cancers worldwide with intestinal obstruction being the most common presentation bleeding and perforation the management of such condition it's either by an elective or emergency surgery and the decision is made according to the type of presentation and the status of patient wellbeing our study will compare between the two types of management at Medical city complex in Baghdad. **Study design:** This is analyticalretrospective study including 123 patients who underwent surgeries for colorectal cancers from 2012 to 2015 at both Baghdad and GIT teaching hospitals. All tumors were re-evaluated using a standardized protocol that included information on patient gender, age at operation, Information on tumor location and multiple co-existing tumors was gathered from the original pathological report. The operative results of patient's undergone emergency surgery were compared with those of patient's undergone elective surgery. **Results:** 71 patients had undergone emergency surgery, and only 47 undergone an elective surgery). The majority of patients (71 cases) presented with intestinal obstruction followed by bleeding and perforation. Most patients where men 56% with mean age of 59.2 yrs. In the emergency surgery group the tumor was founded at the level of sigmoid colon while most of the elective surgery group the tumor was founded at the level of rectum. 45 of 76 emergency patient's undergone Hartman procedure and 30 of 47 elective patients treated with Resection and end to end anastomosis. **Conclusions:** This study showed that The emergency group had a higher frequency of multiple tumors and a more aggressive histopathologic profile and more advanced ,and it's more safe to deal with emergency presentation of colorectal cancer in two steps surgery than one step, while this is not in elective cases according to follow up of patient we couldn't find a major differences between the right side of colon and the left side of colon because the Because the distribution of emergency and elective cases was essentially the same between the right and the left colon.

## Introduction:

Colorectal carcinoma (CRC) is the third most common form of cancer worldwide. The most common presentation being obstruction (78% which also include constipation and loss of weight), bleeding (10%) or perforation(4%)<sup>[1, 2]</sup> Rectal cancers seldom present as an emergency (5.9%), whereas this is much more likely with colonic cancers (21.7%)<sup>[2]</sup>. The left colon and the sigmoid are the most common sites of tumor obstruction, but the risk for obstruction seems to be highest at the splenic flexure<sup>[3]</sup>. The cecum have been reported to be the most common sites of perforation, due to blind loop mechanism<sup>[4]</sup>. Other site for Perforation , either at the site of the tumor or proximal to it, and it is a serious condition that, apart from the risk of tumor cells seeding, can result in generalized peritonitis or abscess formation. Patients undergoing acute surgery are generally older than elective cases (mean age 68.6 and 66.3 years, respectively)

and some studies have shown a female predominance (50.3% and 43%, respectively). Both young (<40 years) and old (>80 years) patients with CRC more often present as an emergency<sup>[2,4]</sup>.

Many studies report a poorer outcome for patients who undergo emergency surgery, both during their initial hospital stay and for their long-term survival<sup>[5, 6]</sup>. Emergency surgery for CRC is associated with a higher risk for metastatic disease, possibly because of occult liver metastases, although such cancers do not necessarily show a higher rate of local recurrence<sup>[6, 7]</sup>. In one study, the 5-year overall survival rate following emergency surgery was 39.2%, compared with 64.7% for elective cases<sup>[2]</sup>, and a median survival time of 59 months for emergency compared with 82 months for elective surgery has also been reported<sup>[8]</sup>. Advanced tumor pathology and tumors with unfavorable histologic features may be reasons for this difference in outcome.

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Patients undergoing emergency surgery tend to have more advanced cancers (American Joint Committee on Cancer (AJCC) stages III and IV), with more tumor T3 and T4 tumors and more node (N)1 and N2 cases compared with electively managed patients<sup>[9]</sup>. According to some studies, on a stage-for-stage analysis, the survival rates remain lower for emergency cases even after sub-stratification for factors such as lymph-node status and presence of extramural lymphovascularinvasion<sup>[2,4]</sup>.

R1 resections are also more common among cases presenting as a surgical emergency (10% versus 1%)<sup>[9]</sup>. Many studies have found no difference in the morphological profiles of emergency and elective CRCs<sup>[8,10]</sup>. However, in one study, extramural venous invasion was more common in emergency cases (20% versus 6%), and the survival of patients with obstructive CRC has been linked to the presence of a mucinous tumor<sup>[11]</sup>. Although Abdelrazeq et al. found that perforated tumors were more likely to present with distant metastases, they also found that these tumors were less likely to be poorly differentiated and had less lymph-node involvement<sup>[6]</sup>.

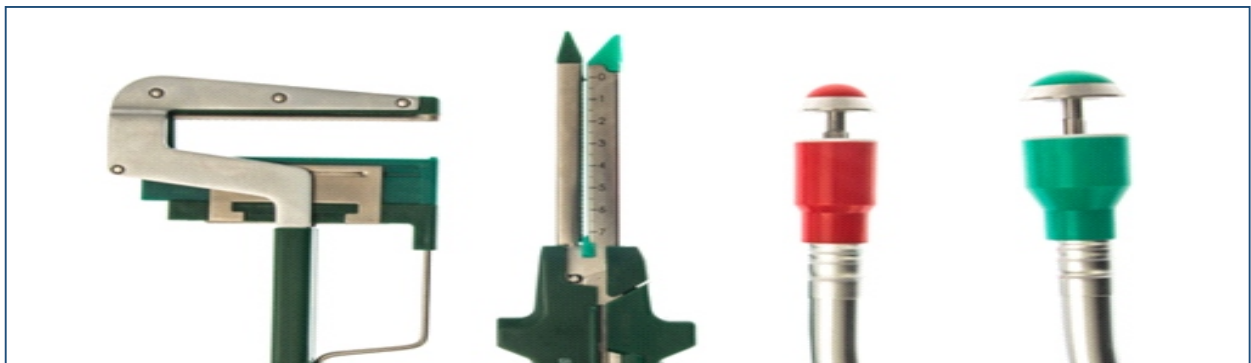
These findings are difficult to interpret, but could indicate that there is a histologic explanation for the poorer surgical outcome in tumors presenting as an emergency compared with elective cases.

In a previous study, we found that there is a 'right-sided' type of colonic cancer, with features such as larger tumor size, higher T and AJCC stage, poor differentiation, and circumscribed tumor margin.<sup>[12]</sup> The 'left-sided' type of colonic cancer and rectal cancer share similar features, with smaller tumor size, lower T and AJCC stage, and infiltrating tumor margin<sup>(12,13)</sup>.

#### ***Double-stapler technique in colorectal surgery:***

Colorectal surgery has evolved significantly in the last 35 years. The introduction in 1975 of surgical staplers (mechanical suture) in Russia mainly for low pelvic anastomosis has had a positive impact<sup>[14]</sup>. The circular stapler has allowed surgeons to perform safer anastomoses at the level of the middle third and lower portion of the rectum, without increasing the occurrence of leaks or anastomotic recurrence in resections due to rectal cancer<sup>[15]</sup>.

Figure 1 : Surgical Staplers (linear, circular, cutting stapler)



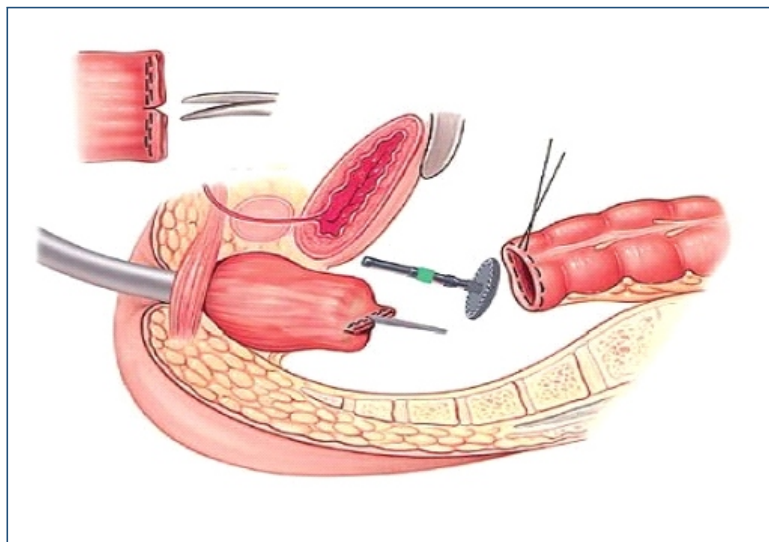
This decreases surgical time in comparison with manual anastomoses and improves quality of life with the possibility of sphincter preservation, mainly with cancer of the middle third and lower portion of the rectum as well as for intestinal inflammatory disease. Other advantages associated

with mechanical suture are a larger diameter of the anastomosis, **less involvement and tension of the tissues**, as well as inversion of the anastomotic margin which decreases complications and above all **it decreases dehiscence** because it favors the scarring process.

Figure 2 : Disposable Hemorrhoids Stapler



Figure 3: intestinal anastomosis using surgical stapler



**Patients and methods:**

Baghdad and GIT teaching hospitals participated in the study. In total, 123 consecutive patients treated surgically for CRC between 2012 and 2015 were assessed for the study. Exclusion criteria included patients that their medical information were lost.

While in the study group, Medical records containing information on type of operation could be found for all. Patient with recurrent colorectal cancer were excluded from the study, also patients with neoadjuvant therapy.

Figure 4: Medical city complex



Recruitment of patients was carried out either by the individual surgeons after surgery or by us, using a list provided for this study. All patients who included in the study, had agreement from either oncologist or surgeon which are responsible about their treatment. A family history of cancer were taken from all study participants, and all CRC diagnoses in the family were verified by medical records.

In this study, an emergency case were defined as a patient who underwent emergency CRC surgery because of perforation, obstruction, or bleeding, regardless of the time elapsed from hospital admission to operation. Most cases were discussed at a post-operative multidisciplinary consensus conference, where they were classified as having undergone emergency or elective surgery. Perforation was defined as pneumoperitoneum on preoperative radiography. Obstructive tumors were defined as tumors causing ileus, regardless of whether the occlusion was partial or complete. Bleeding was defined as blood loss from the tumor causing such severe anemia that the patient had to be treated surgically.

Data on gender, age, and tumor location were obtained for all cases. It was possible to obtain information about family history of CRC. Familial CRC was defined as patients with one or more first-degree or second-degree relatives with CRC, who

did not fulfill the Amsterdam criteria for Lynch syndrome (LS) or who had evidence of heredity for familial adenomatous polyposis (FAP). Three patients with LS were found in our sample, but no case of FAP. All tumors were re-evaluated using a standardized protocol that included information on patient gender, age at operation, Information on tumor location and multiple co-existing tumors was gathered from the original pathological report. All macromorphologic parameters, including tumor size in three dimensions, were obtained from the original pathological report. The number of positive and negative lymph nodes and the number of blocks taken (including large sections) were noted. The micromorphologic parameters assessed were tumor grade, stage, medullary features, mucin production, mucinous type, tumor-infiltrating lymphocytes (TILs), desmoplasia, tumor necrosis, vascular invasion, perineural growth, budding, and type of tumor margin. Because of preoperative radiotherapy, rectal cancers were omitted from the analysis of necrosis, desmoplastic reaction, and budding. The statistical analysis for assessing clinical significance was done by using P-value and was analyzed by Chi-square and Mann Whitney tests. The statistical results are converted to tables to simplify their study.

**The aim of this retrospective study:**

The aim was to compare the clinical and pathologic profiles of CRC cases, treated surgically either as an emergency or electively, with gender, age group, tumor location, and family history of CRC.

**Results:**

The total number of patients examined was 123, of whom 17 had multipleco-existing cancers. Most of cases were emergency (76 patients)and were elective in 47 cases.

The indication for surgery was found in the medical records: (n = 14) because of perforation, (n = 71) because of obstruction, and (n = 19) because of

bleeding. Constipation, weight loss and other (non-GIT related sign and symptoms) were in 19 patients.

Of the 123 patients, 56% were men (n = 69) and 44% were women (n = 54). Mean age was 59.2 years (range 20-95 years),

The majority (77.4%) of cases were sporadic CRCs (n = 86) and 20.5% were familial (n = 30). Eight cases were known to have LS based on the Amsterdam criteria or screening; 7 of these were in the elective group and 1 in the emergency group.

Table (1) Classification of Presentation in patient with colorectal cancer, in 123 patients included in the study.

<i>Presentation</i>	<i>Emergency</i>	<i>Elective</i>	<i>Total</i>
<i>Obstruction</i>	54	17	71
<i>Bleeding</i>	8	11	19
<i>Perforation</i>	14	-	14
<i>Constipation ,loss of Wt. and other</i>	-	19	19
<i>Total No. of Patient</i>	76	47	123

Table (2) relation to nature of surgery, gender, age group, tumor location, and family history.

	<i>EMERGENCY</i>		<i>ELECTIVE</i>	
<b>GENDER</b>	<b>40 male</b>	<b>36 Female</b>	<b>29 male</b>	<b>18 female</b>
<b>FAMILIAL</b>	20		17	
<b>SPORADIC</b>	56		30	
<b>COLON</b>	61		17	
<b>RECTAL</b>	15		40	

<b>AGE</b>	20-30Y	30-40	40-50	50-60	60-70	>70Y
<b>EMERGENCY</b>	4	8	23	18	10	13
<b>ELECTIVE</b>	1	3	3	10	19	11

Table (3) show the tumor localization distributions for the elective and the emergency group.

SITE OF TUMOR	EMERGENCY (76)		ELECTIVE (47)	
	N	%	N	%
<i>CECUM</i>	(18)	24 %	(6)	13.4 %
<i>ASCENDING COLON</i>	(6)	8.5 %	(5)	9.2 %
<i>HEPATIC FLEXURE</i>	(4)	5.2 %	(2)	4.9 %
<i>TRANSVERSE COLON</i>	(8)	10.1 %	(2)	4.4 %
<i>SPLenic FLEXURE</i>	(4)	5.5 %	(2)	2.8 %
<i>DESCENDING COLON</i>	(6)	7.5 %	(2)	3.3 %
<i>SIGMOID COLON</i>	(28)	36.1 %	(11)	23.3 %
<i>RECTUM</i>	(2)	3.1 %	(18)	38.7 %

Table (4) Types of surgery done in patient with colorectal cancer

TYPE OF SURGERY	RESECTION(END TO END ANASTOMOSIS ± STOMA)	HARTMAN'S PROCEDURE	PALLIATIVE PROCEDURE*
EMERGENCY	11	45	20
ELECTIVE	30	6	11

\* Palliative surgery included (nothing to do, biopsy, diversion stoma like ileostomy or colostomy).

**Table (5) Univariate comparison of clinical and pathologic features in cases of colorectal cancer treated surgically on electively and as an emergency.**

FEATURE	EMERGENCY	ELECTIVE	P-VALUE
> 1 TUMOR	13	4	0.001 significant
MEAN TUMOR DIAMET MM	48	47	Not significant
AJCC STAGE			
I	6	13	0.001
II	10	17	0.002
III	36	8	>0.0001
IV	24	9	>0.0001
T			
1	4	17	0.001
2	10	12	0.72
3	32	10	0.002
4	30	8	0.003
N			
0	10	33	0.002
1	17	7	0.003
2 OR 3	49	7	0.0001
PROPORTION OF POORLY DIFFERENTIATED TUMOR %	15.6%	7.7%	0.21
HISTOPATHOLOGICAL STUDY			
MUCIN PRODUCTION			
0 %	56.6	62.4	///
0-50%	25.6	24.2	0.49
>50%, MUCINOUS TYPE	17.8	13.4	0.14
MUCIN TYPE, IF MUCINOUS, %			
EXTRACELLULAR	69.8	88.3	///
SIGNET RING TYPE COMPONENT	30.2	11.7	0.001
CROHN LIKE LYMPHOCYTIC REACTION, %	69.8	59.8	0.03
TUMOR INFILTRATING LYMPHOCYTE (TIL) %	88.4	70.7	///
<30/10 HPFS	9.6	19.3	///
>30/10 HPFS	90.1	82.6	0.04
DESMOPLASIA %	61.7	66.3	0.03
NECROSIS %	37.7	22.2	0.33
VASCULAR INVASION	28.6	16.6	0.0001
PERINEURAL INVASION	45.5	40	0.001
BUDDING %	45.5	40.0	Not significant
TUMOR MARGIN %			
CIRCUMSCRIBED	41.9	54.5	///
INFILTRATIVE	58.1	45.5	0.008

\*S means P value significant (<0.05)

\*\*NS means P value not significant (>0.05)

\*HS means P value highly significant (<0.01)

\*AJCC American Joint Committee on Cancer, HPF high-power field, N node, T tumor, TILs Tumor-infiltrating lymphocytes.

\*Rectal cancers were omitted from the analysis of necrosis, desmoplasia, and budding because of preoperative radiotherapy

Table (6) Type of anastomosis

TYPE OF ANASTOMOSIS	EMERGENCY (11)	ELECTIVE (30)	CLOSURE OF COLOSTOMY(51)
STAPLER TYPE	5	10	43
COMPLICATION OF STAPLER TYPE	(3)53%	(2)11%	(3)6%
HAND SEWN TYPE	6	20	8
COMPLICATION OF HAND SEWN TYPE	(3)44%	(18)9.2%	(1)4.8%

\*Complication like fistula and leak, abscess collection, others.

\*Complication in emergency, included one step surgery.

### Discussion:

The novel finding of this study is that the cases of CRC treated surgically as an emergency are more likely to have multiple tumors. It's not clearly found in the results.

Emergency tumors tended to be of higher AJCC stage (II to IV), T stage (T4), and N stage (N1 to 2/3) which is in line with previous reports<sup>[2,7]</sup>. This is not unexpected as T stage and AJCC stage reflect the local advancement of the tumor.

In our study significant rate of patient with emergency surgery ,had age between 40-50 years ,and this not correspond with previous studies that said younger and older age group were commonly presented with emergency presentation<sup>(2,3,15)</sup>.

Common site for tumor in our study were the sigmoid in patient with emergency presentation of colorectal cancer (34.1 36.1%), and the rectum in patient with elective management (38.7%), this goes with previous study about colorectal cancer<sup>(15,16)</sup>.

It seems reasonable that locally advanced tumors, by infiltrating through the bowel wall, could promote perforation. A locally advanced tumor would also be more likely to display vascular and perineural invasion, which, in fact, was seen in our study (P = 0.001 and P<0.0001 respectively). Lymphovascular invasion in turn, would increase the probability of lymph node metastases, as indicated by the N stage.

Interestingly, there was no difference in mean tumor diameter between the emergency and the elective groups, nor was there any difference in the frequency of mucinous tumors or tumors showing necrosis. Large mucinous or necrotic tumors would be expected to be more disposed to causing obstruction or perforation, resulting in emergency surgery<sup>[17]</sup>.

The perforations associated with colon cancer are mainly due to a direct mechanism of local destruction at the site of the tumor, which does not

Necessarily mean that the tumor itself has to reach a certain size to achieve this destruction. In about one-third of the cases of perforated colon, the perforation is located proximal to the cancer<sup>[18]</sup>. This is a condition familiar to colorectal surgeons, which is attributed to a diastatic widening of the cecum, eventually leading to perforation. This is often the case in left-sided (sigmoid) tumors. Because of the consistency of the stools in this region, these cancers are prone to cause an obstruction, which in turn leads to dilation of the proximal part of the colon. The law of La Place states that the site of largest diameter requires the least pressure to cause distention. Hence, the cecum is the most vulnerable part of the colon, and will perforate at a certain diameter, usually described as 130 mm in the literature if there is an obstructing distal tumor in the left colon<sup>[19]</sup>.

Presence of a mucinous tumor with signet-ring cells was more frequent in the emergency group. This type of mucin-producing tumor, with mucin pools filled with cells displaying a large cytoplasmic mucin vacuoles, might make the tumor less cohesive and firm, and thereby more prone to perforation.

Signet-ring cell carcinomas comprise only 0.7 to 2.6% of all CRCs. Compared with other adenocarcinomas ,these tumors have a poorer prognosis with higher rates of distant recurrence and lower rates of survival, in our study signet ring cell were found in (30, 11 %) in emergency and elective surgery ,respectively<sup>[20,21]</sup>.

We found tumors with TILs more than 30/HPF to be more common in the emergency compared with the elective group. A large number of TILs is a distinct feature of the so-called microsatellite instability (MSI)-CRC phenotype, which is seen in most cases of LS and in approximately 12 to 17% of sporadic CRCs. MSI tumors have a unique clinical picture and



Pathologic phenotype, with a better prognosis and a different response to chemotherapy<sup>[10-22]</sup>. Approximately 30% of right-sided CRCs are shown to be of the MSI type, and the majority of MSI tumors are located on the right side<sup>[21,23]</sup>. The most common reported site of obstruction is the sigmoid colon which might explain the under-representation of tumors with a large number of TILs among our emergency cases<sup>[24]</sup>.

Regardless of MSI status, lymphocyte invasion may reflect an anti-tumor immune response<sup>[25]</sup>. In CRCs treated surgically as an emergency because of perforation, this cellular reaction might not have had time to develop. Three MSI-associated features, namely multiple tumors, signet-ring cell carcinomas, and a Crohn-like lymphocytic reaction, were more common in the emergency group, whereas a large number of TILs and a circumscribed tumor margin were more common in the elective cases<sup>[26]</sup>.

As mentioned above, vascular invasion was more common in the emergency cases in our study. It seems likely that emergency tumors, being more locally advanced, will show a higher frequency of both vascular and perineural invasion. This is reflected in reports showing a worse prognosis for CRCs treated surgically as emergency cases. A higher frequency of vascular invasion should feasibly lead to more distant metastases, but we were unable to assess M stage in our study. A follow-up of our patients over 5 or 10 years could perhaps reveal a correlation between vascular invasion and survival time, as shown in previous studies<sup>[20,24,27]</sup>.

Finally, the emergency cases also displayed a higher frequency of tumors with an infiltrative margin ( $P < 0.0001$ ). This finding is also in accordance with the fact that locally aggressive tumors cause perforation.

We also looked at the effect of gender, age group, tumor location, and family history on the nature of surgical presentation. In a univariate analysis, only tumor location was found to be a significant factor, with a highly significantly lower risk ( $P < 0.0001$ ) of requirement of emergency surgery for a rectal cancer, compared with a right-sided colonic cancer. Different techniques in dealing with colorectal surgery were used (resection with end to end anastomosis, Hartman's procedure and palliative procedures like biopsy  $\pm$  ileostomy or colostomy), in emergency surgery for colorectal cancer, one step surgery was done in 11 patients (3 by stapler), complications like leak were developed in high percentage by two method. in elective surgery including closure colostomy, both methods of anastomosis show very low rate of complications, this reflect that one step surgery in emergency cases associated with higher complication and not safe while in elective cases this is vice versa.

### Conclusions:

Several differences were found between CRCs treated surgically as an emergency and those treated electively. What are ??

The emergency group had a higher frequency of multiple tumors and a more aggressive histopathologic profile and more advanced stage.

Because the distribution of emergency and elective cases was essentially the same between the right and the left colon, the observed differences cannot primarily be attributed to differences in macro-environment or tumor location between the two groups.

It is known that emergency colorectal surgery is associated with a poorer outcome and higher recurrence and mortality rates. This has traditionally been considered to be a technical and surgical problem, consequently leading to a more frequent use of adjuvant chemotherapy in such cases. Our study suggests that the complexity of this issue probably involves a more aggressive nature of the tumor itself.

It seems more safe and less complicated to deal with emergency presentation of colorectal cancer in two steps surgery than one step, while this is not in elective cases according to follow up of patients in both group (emergency and elective).

If future studies are able to classify the genetic background of these tumors then more precise and adequate colon cancer treatment will become more feasible.

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