Prognostic factors and outcome of surgical management and adjuvant chemotherapy of advanced stage colorectal cancer: a single institution experience

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Abstract:

Introduction: Colorectal cancer is the 3rd common cancer and the 4th cause of cancer-related death worldwide. Stage II and III define locally advanced colorectal cancer while stage IV represents a metastatic stage according to the AGCC staging system. Locally advanced colorectal cancer is more difficult to treat as multi-visceral resection is often required(1).

Patients and methods: Data collected included all clinicopathological features (age, sex, TNM stage, pathological subtype, grade, pre-and post-operative CEA and CA19-9) surgery details (type, organs resected, lymph node status, surgery dates, intraoperative and postoperative morbidity, and mortality) as well as the neoadjuvant or adjuvant therapy (regimen, cycles, toxicity).

Results: Forty-eight procedures (61.5%) were considered curative (R0 resections, without residual tumor and 30 (38.4%) were palliative (R1 resections, with microscopic residual tumor or R2 resections, with macroscopic residual tumor). Most of the cases(n=58cases,74.4%) received adjuvant chemotherapy with an oxaliplatin-based regimen (82.8%) and a toxicity rate of 31.0% (n=18,).

Conclusion: Achievement of R0 resection and negative surgical margin are essential for cure.

The multiorgan resection does not affect the survival outcome.

Only male sex, advanced stage of the disease showed a negative prognostic factor with the overall survival while adjuvant chemotherapy is a good prognostic factor for a better survival outcome. National screening programs should be implemented to help diagnosing colorectal cancers in earlier stages and achieve cure with the least intervention.

Keywords:
Surgery, Adjuvant therapy, Colorectal cancer, advanced stage, outcome, local recurrence, distant recurrence, overall survival, lymph node-negative, lymph node positive.

Received: 22 December 2022
Accepted: 3 January 2023

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Introduction:

Colorectal cancer is the 3rd common cancer and the 4th cause of cancer related death worldwide. Stage II and III define the locally advanced colorectal cancer while stage IV represents a metastatic stage according to the AGCC staging system.

Locally advanced colorectal cancer represents 60 to 70% of all symptomatic cases[2].In Egypt, colorectal cancer is diagnosed in late stages and at a younger age than in other parts of the world[3, 4]. Locally advanced colorectal cancer is more difficult to treat as multi-visceral resection is often required[1]. Functional deficits and surgical complications are more likely to occur, especially when the tumor involves the sphincters as in rectal cancer or treatment necessitates the formation of a permanent or even temporary stoma.

Also, liver metastases in colon cancer can be cured but the presence of multiple metastatic sites carries a bad prognosis with overall survival of stage II, III, and IV in the range of, 91%,72%,14% respectively in colorectal cancer according to SEER data between 2011 and 2017.

Many prognostic factors were identified for colorectal cancer namely the lymph node status, the TNM stage, tumor extent, and lymphatic and neural invasion [5].

We hereby retrospectively review the surgical treatment and drug therapy outcome, and prognostic factors as primary endpoints of advanced colorectal cancer diagnosed in the NCI for one year period in 2015.

The surgical management, and adjuvant drug therapy, prognostic factors are reviewed, and primary outcome in the form of progression-free and overall survival is calculated.

Patients and Methods:

Medical records and files of patients diagnosed with advanced colorectal cancer (Stage II, III, IV) were reviewed. locally advanced stages of colorectal carcinoma are stage II (T3-4, N0, M0) and stage III (any T, N1-2, M0), metastatic (any T, any N, M1).

Data collected included all clinicopathological features (age, sex, TNM stage, pathological subtype, grade, pre- and post-operative CEA and CA19-9) surgery details (type, organs resected, lymph node status, surgery dates, intraoperative and postoperative morbidity and mortality) as well as the neoadjuvant or adjuvant therapy (regimen, cycles, toxicity).

Diagnosis of colorectal cancer was determined using endoscopic biopsies for all cases. Metastatic workup (CT chest, abdomen, and pelvis), routine labs (CBC, kidney function, and liver function tests). Tumor markers (CA19-9, CEA) were done. Tumors were staged according to the TNM/ AJCC classification(6)

Lymph node evaluation was done using staging CT of the abdomen and pelvis in all cases. The postoperative staging was done for both the primary tumor and the lymph nodes removed.

Upfront Surgery was done if the tumor was deemed operable and resectable and the surgery type was determined by the tumor site. Adjuvant therapy given was in the form of a chemotherapy or radiotherapy if indicated.

Mortality, recurrence and oncological outcome during follow-up were recorded, the minimum follow up duration after completion of all the treatment was one and half year (18 months) and the maximum duration was 104 months.

The final outcome in terms of disease-free survival for stage II, III, progression free survival (an event defined as recurrence, progression or death) for stage IV was calculated from the date of last treatment (surgery or adjuvant therapy to the last follow up date and status for all the patients. Overall survival was determined for all stages of advanced colorectal cancer cases.

Statistical methods:

All data collected were statistically analyzed using the SPSS package version 22. Numerical data were expressed as mean, median, and standard deviation (SD). Qualitative was expressed as frequency and percentage. Chi-square (Fischer exact) test was used to examine the relation between qualitative variables as appropriate.

A descriptive analysis of all clinicopathological parameters of the patients was done. These parameters and surgery type and drug treatment regimen were all correlated. The disease-free and overall survival were calculated and drawn as survival curves. Factors potentially affecting prognosis were then confronted with survival and recurrence rates.

Multivariate analysis was done using Cox-regression method for the significant factors affecting survival on univariate analysis. Hazard ratio (HR) with it 95% confidence interval (CI) were used for risk estimation.

Ethical issues:

The institutional review board was contacted and being a retrospective study, it was exempted.

Protection of privacy and confidentiality:

This study is a retrospective study that does not impose any risk to the patient, data collection and presentation were anonymous and both privacy and confidentiality were protected to the maximum possibility.

Results:

A total number of consecutive 78 patients were diagnosed with locally advanced colon cancer (n=45 cases) and metastatic(n=33) were diagnosed with stage IV. These represent 78 consecutive cases of the total cases of colon cancer diagnosed this year. Seventy % of the patients were aged < 45 years. Female patients represented 51.1%. Comorbidities in the form of hypertension and diabetes represented 31% and 17.1% respectively. Tumor grades 1, 2, and 3 were 5 (11.1%), 22 (48.9%), and 12 (26.7%) respectively. The tumors were staged by the AGCC staging system with T3, and T4 representing 31.8% cases respectively. Upon the grouping of the TNM stages,40 cases were considered stage III while 33 cases were stage IV. Most of the tumors were adenocarcinomas (83.3%). Clinicopathological characteristics are shown in table (1)

Forty-eight surgical procedures (61.5%) were considered curative (R0 resections, without residual tumor and 30 (38.4%) were palliative surgeries (R1 resections, with microscopic residual tumor or R2 resections, with macroscopic residual tumor).

Terminal Colostomies were necessary in 10 patients after abdominoperineal resection, proctocolectomy and posterior pelvic exenteration. Defunctioning ileostomies were performed in 6 (33%) patients after low anterior resection. neoadjuvant chemoradiation (5400 Gy, 5-Fluoracil and leucovorin) was only indicated to mid or distal rectal tumors (4/22 rectal tumors: 18.1%). Techniques of proctectomy included total mesorectal excision.

Multiple organ resection was done in 16 cases (20.5) with mostly the uterus and ovaries removed in 10 cases. The urinary bladder resected partially in one patient, posterior pelvic exenteration done in 4 cases.

Nephrectomy (1 case), partial gastrectomy (2 cases), cholecystectomy (2 cases).

Metastatectomy was done in three cases only (4.4%). The most common metastatic site was the liver (35.9%) followed by the lung (6.5%) in stage IV cases. The surgical procedures and adjuvant treatment are listed in table (2).

Adjuvant therapy:

The majority of the cases(n=58cases,74.4%) received adjuvant chemotherapy with oxaliplatin-based regimen (82.8%) and a toxicity rate of 31.0% (n=18,).

Histological features:

According to the depth of penetration and Dukes classification, Duke's B were 29(37.1%) and Dukes C 49 cases (62.8%).

Lymph node involvement was detected in 36 patients (67%), 21 (46.7%) in the locally advanced group and 15 patients (68.2%) within the metastatic group. The number of positive lymph nodes were more than 15 lymph nodes in 52.1% and less than 15 positive nodes in 47.9% of cases.

The lymph node positivity increased with stage advancement being 68.2% in stage IV and 46.8% in locally advanced stages.

Clinicopathological characteristics, histological features, surgical treatment and adjuvant treatment for stage II, III, IV are shown in table (2).

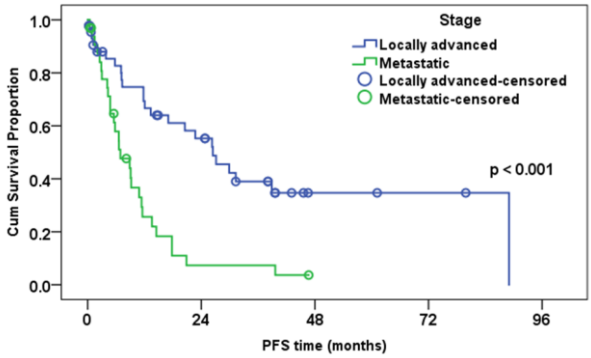
Survival and recurrence

Length of follow-up among all patients at all stages varied from 18 to 140 months, and there was not statistical difference between colon and rectal lesions.

At the end of this study, 41.0% of the cases were alive while 58.8% died. In the locally advanced stage, 23 patients had out of 45(48.9%) compared to 24 events out of 33 patients (27.3%) in stage IV. The cumulative survival at 18 months and 104 months in the locally advanced stage were 73.2% and 32.7% respectively. While in the metastatic stage the cumulative survival at 15 and 103 months were 38.8% and 16.8% respectively. The median follow-up time range from 20 months to 89.01 months. The maximum follow-up duration was 140 months. The median overall survival for all stages is 23.8% with 60.3% and 13.4% median overall survival in the locally advanced and metastatic stages respectively(p-value:0.004).

Progression of disease occurred in 28 cases out of 33 cases in the metastatic stage (15.2%) and 24 events occurred out of 45 cases (46.7). The progression-free survival (recurrence or progression or death) achieved for all stages was 33.3% (N=52).

The PFS and overall survival curves are shown in figures (1) and (2) respectively.



Progression free survival (PFS): events are recurrence or progression or death.

Figure (1): progression free survival curve

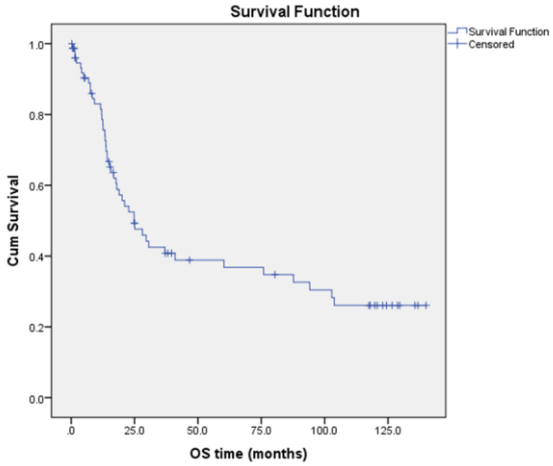


Figure (2): Overall survival curve of the studied group

Prognostic factors:

On multivariate analysis using Cox-proportional hazard model; Male Patients had worse overall survival compared to females (HR: 3.2 [95%CI:1.6-6.4), p=0.001.

Patients with stage IV had worse overall survival compared to those with stage II & III (HR: 3.1 [95%CI:1.4-6.6), p=0.004.

Patients who did not receive adjuvant chemotherapy had worse overall survival compared to those who received adjuvant chemotherapy (HR: 2.7 [95%CI:1.1-6.6), p=0.029)

None of the other variables had any correlation with overall survival (OS) or progression free survival.

Overall Survival curves correlated with sex, stage and adjuvant chemotherapy are shown in figures (3),(4),(5)and respectively.

Table (1): Characteristics of the cases of stage 2,3,4

Variable		Count	%
Age45	=< 45 yrs	23	29.5%
	> 45 yrs	55	70.5%
Age50	=< 50 yrs	35	44.9%
	> 50 yrs	43	55.1%
Sex	Male	35	44.9%
	Female	43	55.1%
DM	No	62	79.5%
	Yes	16	20.5%
HTN	No	65	83.3%
	Yes	13	16.7%
FH	No	72	92.3%
	Yes	6	7.7%
Double Primary	No	77	98.7%
	Osteosarcoma	1	1.3%
	Laryngeal cancer	0	0.0%
Preoperative CEA	N	21	50.0%
	High	21	50.0%
Preoperative CA19.9	N	19	50.0%
	High	19	50.0%
Tumor Site	Left Colon	26	33.8%
	Rectum (22 cases total)	18	28.6%
	Upper rectum	4	
	Mid and low rectum		
	Right, transverse Colon	29	37.7%
Pathology subtype	Adenocarcinoma	65	83.3%
	Mucnious Adenoca	13	16.7%
Grade	Grade II	64	82.1%
	Grade III	14	17.9%
Surgical Treatment			
Surgery.type	Right hemicolectomy	20	29.0%
	Left hemicolectomy, rectosigmoidectomy and sigmoidectomy	18	26.1%
	Total colectomy, proctocolectomy	4	5.8%
	LAR	18	26.1%
	APR	3	4.3%
	PPE	3	4.3%
	transverse colectomy	3	4.3%
Metastatectomy	No	75	96.2%
	Yes	3	3.8%
TNM staging of the cases			
T	T1	0	0.0%
	T2	4	6.3%
	T3	44	69.8%
	T4	15	23.8%
LN	LN -ve	31	46.3%
	LN +ve	36	53.7%
M	M0	45	57.7%
	M1	33	42.3%
Liver	No	50	64.1%
	Yes	28	35.9%
Lung	No	73	93.6%
	Yes	5	6.4%
Bone	No	78	100.0%
	Yes	0	0.0%
Nodal	No	77	98.7%
	Yes	1	1.3%
Peritoneum	No	75	96.2%
	Yes	3	3.8%

LN. Total				
		Frequency	Percent	Valid Percent
Valid	=< 15 LN	40	40.0	47.9
	> 15 LN	37	43.5	52.1
	Total	71	83.5	100.0
Adjuvant treatment				
Adjuvant	No		20	25.6%
	Yes		58	74.4%
Adj.RTH	No		64	82.1%
	Yes		14	17.9%
Adj.CTH	No		20	25.6%
	Yes		58	74.4%
Adj.Cth.type	Oxaloplatin based regimens		48	82.8%
	5 FU based regimens		10	17.2%
Toxicity1	No Toxicity		40	69.0%
	Toxicity		18	31.0%
Characteristics of the cases all stages (II,III,IV)				
			Count	Column N %
Age45	=< 45 yrs		23	29.5%
	> 45 yrs		55	70.5%
Age50	=< 50 yrs		35	44.9%
	> 50 yrs		43	55.1%
Sex	Male		35	44.9%
	Female		43	55.1%
DM	No		62	79.5%
	Yes		16	20.5%
FH	No		72	92.3%
	Yes		6	7.7%
Double Primary	No		77	98.7%
	Osteosarcoma		1	1.3%
	Laryngeal cancer		0	0.0%
CEA	N		21	50.0%
	High		21	50.0%
CA19.9	N		19	50.0%
	High		19	50.0%
Surgery.type	Right hemicolectomy		20	29.0%
	Leftt hemicolectomy, rectosigmoidectomy,sigmoid ectomy		18	26.1%
	Total colectomy, proctocolectomy		4	5.8%
	LAR		18	26.1%
	APR		3	4.3%
	PPE		3	4.3%
	transverse colectomy		3	4.3%
Metastatectomy	No		75	96.2%
	Yes		3	3.8%
Tumor Site	Left Colon		26	33.8%
	Rectum		22	28.6%
	Right and transverse Colon		29	37.7%
Pathology	Adenocarcinoma		65	83.3%
	Mucnious Adenoca		13	16.7%
Grade	Grade II		64	82.1%
	Grade III		14	17.9%
T	T1		0	0.0%
	T2		4	6.3%
	T3		44	69.8%
	T4		15	23.8%

LN	LN -ve	31	46.3%
	LN +ve	36	53.7%
M	M0	45	57.7%
	M1	33	42.3%
Lung	No	73	93.6%
	Yes	5	6.4%
Bone	No	78	100.0%
	Yes	0	0.0%
Nodal	No	77	98.7%
	Yes	1	1.3%
Peritoneum	No	75	96.2%
	Yes	3	3.8%
Postoperative	N	63	98.4%
.CEA	High	1	1.6%
Postoperative	N	21	77.8%
.CA19.9	High	6	22.2%
Adjuvant	No	20	25.6%
treatment	Yes	58	74.4%
Adjuvant .RTH	No	64	82.1%
	Yes	14	17.9%
Adjuvant .CTH	No	20	25.6%
	Yes	58	74.4%
Adj.Cth.regimen	Oxaloplatin based regimens	48	82.8%
	5 FU based regimens	10	17.2%
Toxicity of chemotherapy	No Toxicity	40	69.0%

Table (2): Comparison of the clinicopathological characteristics, surgery, adjuvant treatment between Locally advanced (II,III) and metastatic cases.

		Stages				
		Locally advanced (II,III)		Metastatic (IV)		
		Count	%	Count	%	p-value
Age45	=< 45 yrs	16	35.6%	7	21.2%	
	> 45 yrs	29	64.4%	26	78.8%	
Age50	=< 50 yrs	26	57.8%	9	27.3%	
	> 50 yrs	19	42.2%	24	72.7%	
Sex	Male	17	37.8%	18	54.5%	
	Female	28	62.2%	15	45.5%	
DM	No	39	86.7%	23	69.7%	
	Yes	6	13.3%	10	30.3%	
HTN	No	40	88.9%	25	75.8%	
	Yes	5	11.1%	8	24.2%	
FH	No	42	93.3%	30	90.9%	
	Yes	3	6.7%	3	9.1%	
Double Primary	No	44	97.8%	33	100.0%	
	Osteosarcoma	1	2.2%	0	0.0%	
	breast cancer	1	1.0%	0	0.0%	
CEA	N	14	66.7%	7	33.3%	
	High	7	33.3%	14	66.7%	
CA19.9	N	12	66.7%	7	35.0%	
	High	6	33.3%	13	65.0%	
TLC	N	26	96.3%	12	70.6%	
	High	1	3.7%	5	29.4%	
Hb10	< 10	12	44.4%	13	68.4%	
	>=10	15	55.6%	6	31.6%	
Surgery.type	Right hemicolectomy	15	33.3%	5	20.8%	
	Leftt hemicolectomy, rectosigmoidectomy,sigmoid ectomy	9	20.0%	9	37.5%	
	Total colectomy, proctocolectomy	2	4.4%	2	8.3%	
	LAR	11	24.4%	7	29.2%	
	APR	3	6.7%	0	0.0%	
	PPE(posterior pelvic extenteration)	3	6.7%	0	0.0%	
	transverse colectomy	2	4.4%	1	4.2%	
Metastatectomy	No	45	100.0%	30	90.9%	
	Yes	0	0.0%	3	9.1%	
Site1	Left Colon	12	27.3%	14	42.4%	
	Rectum	15	34.1%	7	21.2%	
	Right, transverse Colon	17	38.6%	12	36.4%	
Pathology	Adenocarcinoma	38	84.4%	27	81.8%	
	Mucnious Adenocarcinoma	7	15.6%	6	18.2%	
Grade	Grade II	35	77.8%	29	87.9%	
	Grade III	10	22.2%	4	12.1%	
T	T1	0	0.0%	0	0.0%	
	T2	4	9.3%	0	0.0%	
	T3	31	72.1%	13	65.0%	
	T4	8	18.6%	7	35.0%	
LN	LN -ve	24	53.3%	7	31.8%	
	LN +ve	21	46.7%	15	68.2%	
Peritoneum	Yes	0	0.0%	3	9.1%	
Post	N	37	100.0%	26	96.3%	
operative.CEA	High	0	0.0%	1	3.7%	
Postoperative	N	12	80.0%	9	75.0%	
.CA19.9	High	3	20.0%	3	25.0%	
Adjuvant	No	14	31.1%	6	18.2%	
	Yes	31	68.9%	27	81.8%	
Adj.RTH	No	31	68.9%	33	100.0%	
	Yes	14	31.1%	0	0.0%	
Adj.CTH	No	15	33.3%	5	15.2%	
	Yes	30	66.7%	28	84.8%	
Adj.Cth.regimen	Oxaloplatin based regimens	27	90.0%	21	75.0%	
	5 FU based regimens	3	10.0%	7	25.0%	
Chemotherapy	No Toxicity	20	66.7%	20	71.4%	
Toxicity	Toxicity	10	33.3%	8	28.6%	

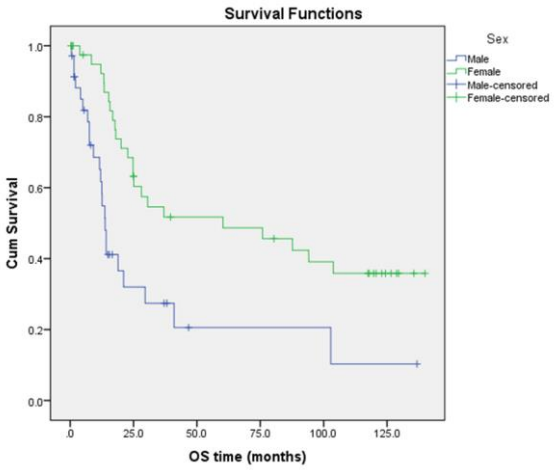


Figure (3): Overall survival and Sex

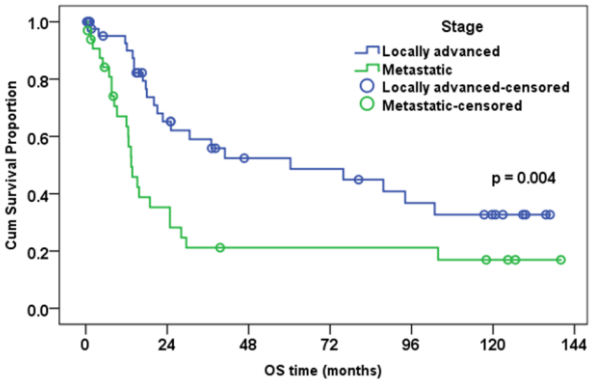


Figure (4): overall survival and stage

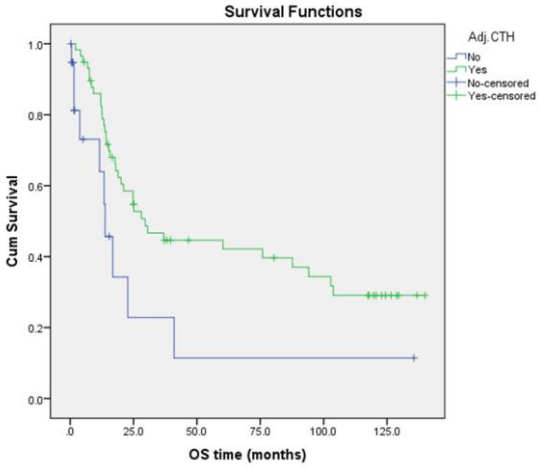


Figure (5): Overall survival and adjuvant chemotherapy

Discussion:

In this study, surgical resection was the main line of treatment for locally advanced colorectal cancer (stages II, III) and in metastatic cases (stage IV) representing 26.6% (N=12 cases) and 62.4% (33 cases) respectively. R0 resection rate of 61.5%(n=62) was achieved for all stages. Multiple organ resection was done in 20.5%(n=16).

Surgery for locally advanced colorectal cancer is challenging and requires surgical skills and multiple organ resections to achieve a cure[1].Resection with no residual (R0) is the goal in locally advanced and metastatic colorectal cancer.[7]. Obtaining a tumor-free margin, and en-bloc resection of any organs or structures attached to the tumor is essential [8].

The extent of resection and the number of organs resected depends upon the site of the primary tumor (right colon versus left colon versus rectal) and the stage[9]. It had been reported that 5 to 22% of colorectal cancer surgeries are for T4 tumors or locally advanced tumors [10].

Our study showed that 66.6% (n=10) of T4 tumors required multiorgan resection. Previous series showed a lower rate (25.4%) of multivisceral resection for locally advanced tumors[9].

Malignant adhesions between resected organs was reported in previous studies to range from 40 to 72.5% of cases [11].Malignant infiltrations of adjacent resected organs was present in 56.2% (n=9) of cases in our study. The difficulty to differentiate inflammatory adhesions from malignancy during surgery forces the surgeon to perform an en bloc resection to achieve an R0,as has mentioned in previous studies most of the clinical T4 tumors are recognized at the time of surgery[12].The most common organs resected are the uterus and adenexae due to proximity to the colon and rectum. The literature have reported prophylactic oophorectomy if in proximity to the primary tumor especially the left ovary in left colonic and rectal cancer[13], this may explain why the ovaries and adenexae are the most common resected organs in our series. Right sided locally advanced colonic tumors are more likely to require extensive resection and, in many cases, they are irresectable due to proximity to the duodenum and the head of the pancreas. In such cases neoadjuvant chemotherapy may be required to achieve downstaging. In our series the kidneys, sleeve gastrectomy, partial urinary bladder resection was resected less frequently. In this study all right sided locally advanced tumors were amenable to resection with right hemicolectomy or extended right hemicolectomy with or without adjacent organ resection except for one case with a residual left at the duodenum and the right kidney. No Neoadjuvant therapy was given for all colonic cases.

Despite that Posterior pelvic exenteration represents an extensive ultra-major surgery with substantial morbidity and mortality, it had been shown in a metanalysis that patients who undergo Pelvic exenteration for advanced or recurrent rectal cancer can

achieve long-term survival (up to 60% at 5 years) with acceptable morbidity and quality of life[14].This procedure was performed in 6 cases in our study.

Surgery remains the principal treatment for stage IV. The liver is the most frequent (approximately 33%) metastatic site (Van Cutsem et al., 2006; Cui et al., 2013). Colorectal liver metastases (CLM) are present in 15% to 25% of cases at the time of diagnosis of the primary tumor (synchronous metastases), and approximately half of the patients undergoing radical resection of CRC will develop metastatic disease (metachronous metastatectomy)[15].

Curative resection of the primary tumor as well as metastatectomy in one setting or in multiple settings can achieve a good survival in this late stage of the disease with a good survival outcome after metastatectomy[16].In this study complete resection of the metastases and the primary tumor was done in 3 cases. Primary liver metastatectomy and tumor resection was done in 2 cases for synchronous liver metastases and in another patient, left lung lobectomy for metastases was done after resection of the primary colonic tumor. We couldn't correlate metastatectomy with survival due to small number of the cases, however five-year survival after curative resection was reported to range range from 30%-40% (up to 60% in selected series), whereas less than 2% of patients are alive 5 years after diagnosis without surgical therapy[17].

Colorectal tumors with Peritoneal metastasis had long been considered inoperable but now with the cytoreduction surgical technique and tailored or complete peritonectomy and hyperthermic intraperitoneal chemotherapy (HIPEC), a survival of 27% 5 year survival can be achieved [18]. None of our cases received HIPEC as this technique was introduced in our Institute after the study period.

When metastases cannot be resected either primarily or secondary, resection of the primary colorectal tumor can be done as a palliative procedure. With the advancement in surgical techniques and neoadjuvant drug therapy, one stage or multistage resection can be done especially with liver metastases or peritoneum as the only metastatic sites.

The extensive surgery and the multiorgan resection are not without morbidity since it mandates the formation of permanent stoma in total Colo proctectomy and abdominoperineal resection or even covering ileostomy in high risk anastomoses with low anterior resection.

In this study there were no intraoperative or postoperative mortality.

Despite that the site of the tumor is considered a main determinant of the extent and type of surgery as well as local recurrence and overall survival, no correlation was found in our patients between the extent of resection, type of surgery or site of the tumor with the overall survival or progression free survival.

Many studies reported a better survival outcome related to the site of the tumor, with the rectal site having a worse survival compared to the right and left colon[1].

The more the tumor is advanced locally, more organ resection is needed, and the tumor is more prone to present with obstruction or perforation and the need to perform a transient or a permanent stoma.

In our study, the overall survival and the progression-free survival were not dependent upon the site of the tumor, the colon or the rectal site when compared stage by stage.

overall survival for all stages in this series is 23.8% and median overall survival in the locally advanced and metastatic stages were 60.3% and 13.4% respectively (p-value:0.004).

One of the most important predictors of outcome in advanced colorectal cancer is the stage[5]. On multivariate analysis, stage was correlated with the PFS and OS.

This is in concordance with published literature that states that stage is an independent prognostic factor in colorectal cancer[5].

Lymph node status is part of the TNM staging system and of the DUKE and Astler Coller classification of colon cancer. Lymph node positive tumors and the number of retrieved lymph nodes is associated with higher tumor stage, tumor size, and right-sided location and tend to have a worse overall PFS and OS [19]. We couldn't find such a correlation in our study separately from the stage contrary to published literature.

Male sex was an independent prognostic factor in this study. It was reported that males have a worse overall survival in colorectal cancer in concordance with our results.

In locally advanced colorectal cancer (stage III) adjuvant chemotherapy with fluorouracil plus leucovorin for six to eight months is standard treatment. It decreases the risk of death by one third[20].

Local recurrence and overall survival (OS) are better with adjuvant chemotherapy. Our results show that patients who received adjuvant chemotherapy irrespective of the regimen given had a better overall survival.

This study is limited by its retrospective nature and small sample size and the lack of the cases that were treated with cytoreduction and HIPEC, since this technique represents the new advancement in locally advanced and metastatic peritoneal colorectal cancer.

Conclusion:

Locally advanced and metastatic colorectal cancer represents a challenge to the surgeon due to the need of more extensive surgery and multiple organ resection.

In metastatic cases, one stage resection or multistage resection of the metastasis can be done.

Achievement of R0 resection and negative surgical margin are essential for cure.

The multiorgan resection does not affect the survival outcome.

Only male sex, advanced stage of the disease showed a negative prognostic factor with the overall survival while adjuvant chemotherapy is a good prognostic factor for a better survival outcome. National

screening programs should be implemented to help diagnosing colorectal cancers in earlier stages and achieve cure.

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