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ORIGINAL ARTICLE

Clinical Outcome of Laparoscopic Colorectal Resection after Neoadjuvant Chemo-Radiotherapy for Colorectal Carcinoma

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ABSTRACT

Introduction **:N**eoadjuvant chemo-radiotherapy has the advantages of decrease local recurrence rate , deceasing toxicity , down_staging the tumor and minimize rate of mobidity **.**

Methods: Patients were divided into 2 groups in accordance type of preoperative Therapy ,Group 1: included 30 patients comprised those who had colorectal carcinoma with laparoscopic intervention without neoadjuvant therapy**,**Group 2: included 30 patients comprised those who had colorectal carcinoma with laparoscopic intervention with neoadjuvant therapy, This study included patients with colorectal carcinoma were admitted to Zagazig University Hospital & Gastrointestinal surgery center (Mansoura university). Cases were collected in the period from December 2016 to April 2018. The study was approved by the research and Ethics committee of Zagazig University & Mansoura university. a written informed consent was obtained from all participating patients after explaining to them all the study procedures with its benefits and hazards.the work has been carried out in accordance with the code of ethics of the world medical association (Declaration of Helsinki) for studies involving humans.

Results: the results showed that there are significant differences between laparoscopic colectomy with neoadjuvant chemo-radiotheropy and those without neoadjuvant therapy in cases of rectal carcinoma while in cases of colon cancer there are no significant differences . laparoscopic colectomy has more advantages than open surgery in early ambulation , decrease time in staying in hospital , early return to work .

Conclusion: Laparoscopic colorectal resection after neoadjuvant chemo-radiotherapy has higher conversion rate & longer duration of surgery.Mortality & morbidity are equal in both groups

Keywords: Laparoscopic Colectomy, neoadjuvant therapy, Cancer Colon.

INTRODUCTION

Colorectal cancer is considered one of the most common malignancy worldwide and the one of the most common leading cause of deaths **(1).** laparoscopic colectomy has more advantages than open surgery in early ambulation , decrease time in staying in hospital , early return to work and deceasing postoperative pain.

(2). Noeadjuvant therapy has become a gold standard treatement of locally advanced colorectal cancer. It can decrease tumor size leading to compelet resection (R0) , decease the toxcicity and minimize local recurrence rate. Neoadjuvant therapy improves patients survival rate espically in patients with metastatic colorectal cancer **(3).**it decreases the risk of recurrence in patients with high risk findings

during surgery**.** **N**eoadjuvant chemo-radiotherapy has the advantages of decrease local recurrence rate , deceasing toxicity , down_staging the tumor and minimize rate of mobidity over the adjuvant therapy**(4).**

Objectives:

to assess the effect of neoadjuvant chemoradiotherapy on clinical outcome and feasibility in patients were subjected to laparoscopic colorectal excision for colorectal cancer.

PATIENTS AND METHODS

This study included patients with colorectal carcinoma were admitted to Zagazig University Hospital & Gastrointestinal surgery center (Mansoura university). Cases were collected in the period from December 2016 to April 2018. The study was approved by the research and Ethics committee of Zagazig University & Mansoura university. a written informed consent was obtained from all participating patients after explaining to them all the study procedures with its benefits and hazards.the work has been carried out in accordance with the code of ethics of the world medical association (Declaration of Helsinki) for studies involving humans.Patients were divided into 2 groups in accordance type of preoperative Therapy**.**Group 1**:** included 30 patients comprised those who had colorectal carcinoma with laparoscopic intervention without neoadjuvant therapy. Group 2: included 30 patients comprised those who had colorectal carcinoma with laparoscopic intervention with neoadjuvant therapy.

Inclusion criteria:

20 years or older patients. Patient's candidate for laparoscopic surgery (such as patients with no history of abdominal operations).Good general condition of the patients .patients with stage either (I , II , III) colorectal cancer .

Exclusion criteria:

Confirmed late colorectal carcinoma and metastasis by CT or MRI.Complicated colorectal carcinoma eg: perforation, obstruction

Perioperative measures:

In this prospective cohort study , all patients were subjected to the followings: patients were selected randomly, Full history taking , Complete physical examination , Radiological investigations (US for all cases ,barium enema in some cases to exclude cases with suspected complicated colorectal cancer like perforation & obstruction , CT abdomen & pelvis & chest for all cases to rule out the metastatic cases , MRI in cases of rectal carcinoma & to exclude cases of liver metastasis) , Laboratory investigations including CEA , CBC , liver and kidney functions tests , PT , PTT , INR , Colonoscopy and biopsy. We use the TNM staging system for staging the CRC (table 6).

After pretreatement staging evaluation by (US, CT, MRI) we sent patients in group (2) to receive neoadjuvant therapy by oncologists at Radiotherapy department, faculty of medicine , (Zagazig & Mansoura universities). patients were subjected to conventional fractionation radiotherapy (RT) with concurrent fluoropyrimidine chemotherapy (ie, long-course chemoradiotherapy) for rectal cancer, while patients with colon cancer were subjected to neoadjuvant chemotherapy in the form of fluoropyrimidine (long course chemotherapy) . Withen 6-12 weeks after having neoadjuvant therapy we performed the surgery . number of sessions was varied according to pathological type & stage of the tumor .Preoperative colon preparation: Patients were subjected to nothing per oral for 2-3 days before the surgery , repeated enema & laxative for 2 days before the surgery . neomycine and flagyl were prescribed for the patients 2 days before the surgery.

Surgical techniques :

We performed laparoscopic (right hemicolectomy) , left hemicolectomy , transverse colectomy , sigmoidectomy (figure 3,4) , anterior resection , abdominoperineal resection).

Follow up after surgery and discharge from the hospital:

We examined the patients clinically, made routine laboratory investigations (CEA), took

patients' telephone numbers and made follow up u/s, CT. The patients were followed up for one week, two weeks and one month, 6months post operatively.

Statistical analysis:

The collected data were analyzed by computer using Statistical Package of Social Services version 24 (SPSS),Data were represented in tables and graphs,Continuous Quantitative variables e.g. age were expressed as the mean ± SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number)& relative frequencies (percentage). Suitable statistical tests of significance were used after checked for normality. Categorical data were cross tabulated and analyzed by the Chi-square test, Continuous data were evaluated by Mann Whitney test, Survival was examined by Kaplan-Meier Method. The results were considered statistically significant when the significant probability was less than 0.05 (P <0.05).P-value < 0.001 was considered highly statistically significant (HS), and P-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

Demography of the patients:

The age of patients with laparoscopic colorectal resection without neoadjuvant group is ranging from 18-75 years old with mean 50.4 ± 13.52 years old and 60% of them are male while age in laparoscopic colorectal resection with neoadjuvant chemo-radiotherapy is 54.23 ± 11.38 years old, ranged from 28-75 years old .(table 1)

There were 2 patients with stage I & 18 patients with stage II & 10 patients with stage III in Group (1) while there were 4 patients with stage I & 18 patients with stage II & 8 patients with stage III in Group (2). (table 2)

effect of neoadjuvant therapy in group (2) as regarding downstaging the cancer:

there was only one patient who has downstaging in cases of cancer colon while in rectal cancer there were 7 patients dawnstage from T3 to T2 & 18 patients dawnstage from T2 to T1 & 4 patients dawnstage from T1 to T0. (table 3)

Conversion rate, Intraoperative complication and Post-operative complication among the studied groups :

regarding Conversion rate as it is 30% of Resection without neoadjuvant Vs 43.3% of Resection with neoadjuvant . Complications after laparoscopic colorectal resection among the studied groups. Conversion rate, intraoperative bleeding, intraoperative ureteric injury and post-operative adhesions and post-operative is found (30%, 26.7%, 3.3%, 20%&13.3%) respectively in Resection without neoadjuvant group versus (43.3%, 30%, 6.7% ,23.3% &6.7%) respectively in Resection with neoadjuvant group.(figure 1)

Number of resected LN, operation time and amount of blood loss intraoperative among the studied groups:

number of LN resected among Resection without neoadjuvant group it is 13.63± 2.73, with a range from (8-18). While in Resection without neoadjuvant group mean number of LN resected is 14.96± 3.72, with a range from 8-22 LN resected. operation time in the studied Resection without neoadjuvant group ranging from 100-300minutes with median 165 min, while in the Resection with neoadjuvant group the operation time ranging from 110-185 minutes.**(table 4).**

Hospital stay among the studied groups:

mean of hospital stay among Resection without neoadjuvant group is 5.63± 1.86, with a range from (2-8) days. While in Resection without neoadjuvant group mean of hospital stay is 5.8 ± 2.47, with a range from 1-9 days . hospital stay in the studied Resection without neoadjuvant group ranging from 2-8 days with median 6 days, while in the Resection with neoadjuvant group the hospital stay ranging from 1-9 days.**(figure 2).**

Deaths and need for reoperation among the studied groups:

5 patients (16.7%) died in Resection without neoadjuvant group versus only one patient

(3.3%) died in Resection with neoadjuvant group. Regarding need for reoperation 23.3% vs zero % of patients in Resection without neoadjuvant group versus Resection with neoadjuvant group respectivelyneed for reoperation**.(table 5).**

Table (1): Sociodemographic characteristics of the studied groups

Item	Group (1) (N=30)		Group (2) (N=30)		Test	P-value
	No.	%	No.	%		
Age (years)						
Mean ± SD	50.4 ± 13.52		54.23 ± 11.38		372.500*	0.251 (NS)
Median (Range)	50 (18 – 75)		53.5(28– 75)			
Sex						
Male	18	60.0%	17	56.7%	Fisher exact	1.000 (NS)
Female	12	40.0%	13	43.3%		

**** Mann Whitney U test.***
P < 0.05 is significant.
NS: Not significant.

Table (2) : T.N.M STAGING in both groups:

stage	Group (1)		Group (2)		P value
	no	**%**	**no**	**%**	**0.624 (NS)**
I	2	6.666	4	13.33	
II	18	60	18	60	
III	10	33.33	8	26.66	

Table (3) : effect of neoadjuvant therapy in group (2) as regarding downstaging the cancer:

Downstaging	Cases of cancer colon		Cases of rectal cancer	
	no	%	no	%
T3 change to T2	1	3.33	7	23.33
T2change to T1	0	0	18	60
T1change to T0	0	0	4	13.33

Table (4): Number of resected LN, operation time and amount of blood loss intraoperative among the studied groups

Items	Group (1) (N=30)	Group (2) (N=30)	P- value
Number of resected LN			
Mean ± SD	13.63± 2.73	14.96± 3.72	0.165 (NS)
Median (Range)	14(8-18)	14.5(8-22)	
Operation time(min)			
Mean ± SD	160.83 ± 38.26	147.5±22.96	0.105 (NS)
Median (Range)	165(100-300)	147.5(110-185)	
Amount of blood loss			
Mean ± SD	227.66± 63.11	256.6±78.5	0.161 (NS)
Median (Range)	250(100-320)	250(150-350)	

Mann Whitney U test.
P < 0.05 is significant.
NS: Non-significant.

Table (5): Deaths and need for reoperation among the studied groups.

Item	Group (1) (N=30)		Group (2) (N=30)		Test	P-value
	No.	%	No.	%		
Deaths						
No	25	83.3	29	96.7	Fisher's exact	0.195 (NS)
yes	5	16.7	1	3.3		
Need for reoperation						
No	23	76.7	30	100.0	Fisher's exact	0.011* (S)
yes	7	23.3	0	0.0		

Fisher's exact test
****P < 0.05 is significant.***
NS: Not significant.

Table (6) :T.N.M staging system

Stage	Stage	N	M
0	Tis	N0	M0
1	T1	N0	M0
	T2	N0	M0
IIA	T3	N0	M0
IIB	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1-T2	N1_N1c	M0
	T1	N2a	M0
IIIB	T3-T4a	N1_N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N-N2	M0
IVA	Any T	Any N	M1a
IVB	Any T	Any N	M1b

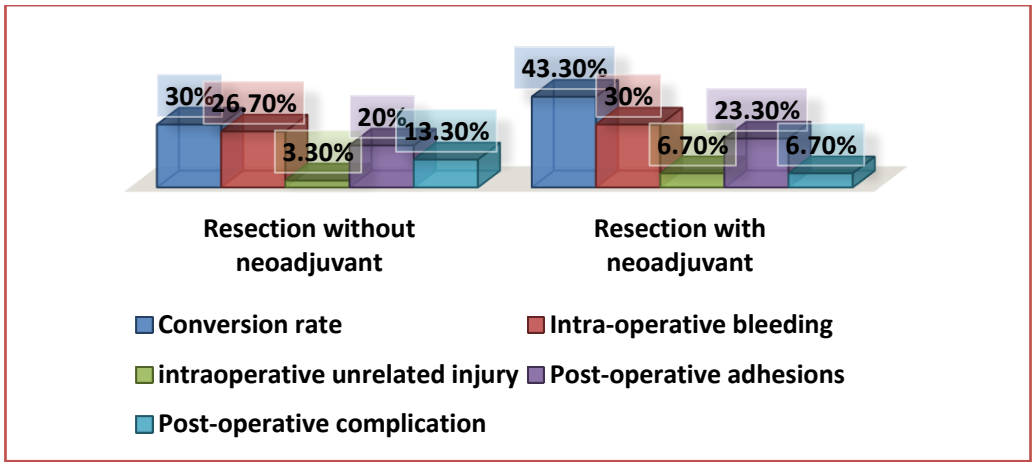


Figure (1): Complications after laparoscopic colorectal resection among the studied groups:

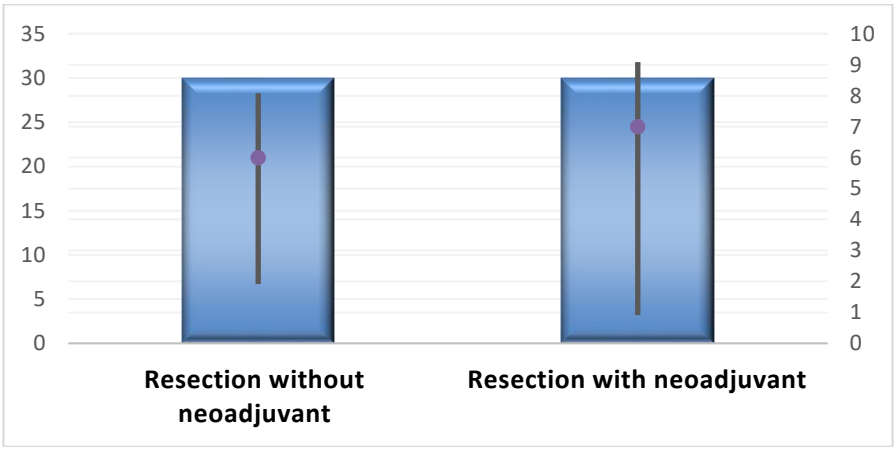
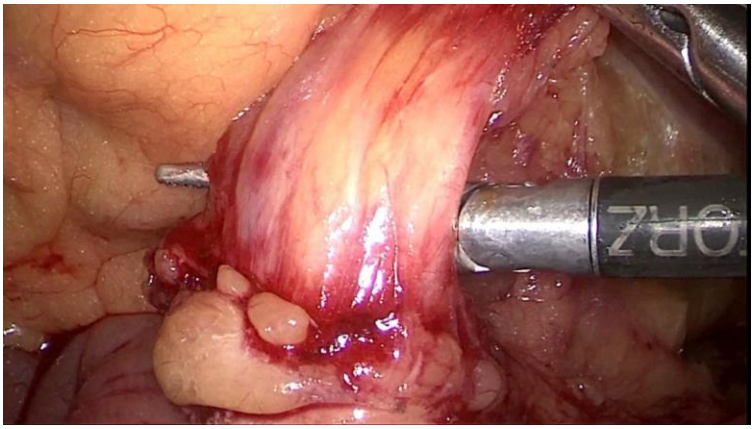
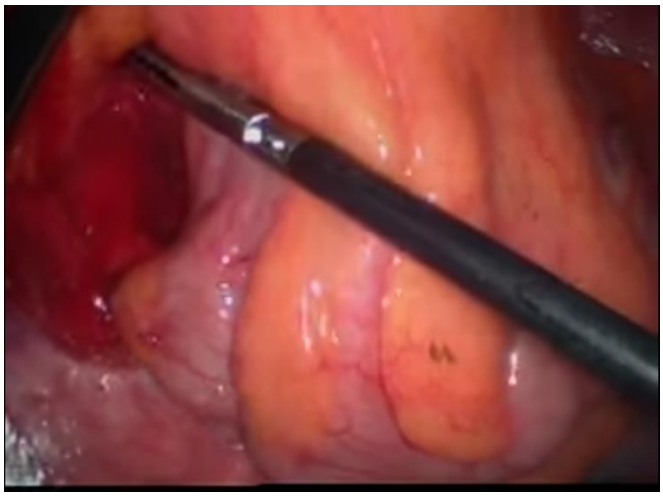


Figure (2): Bar chart for comparison of hospital stay between the studied groups.



Dissection of IMV during sigmoidectomy (figure 3)



Lateral approach dissection during sigmodectomy(figure 4)

DISCUSSION

In our study the age of the patients in group (A) is ranging from 18-75 years old with mean 50.4 ± 13.52 years old and 60% of them are male while the mean age of the patients in group (B) is 54.23 ± 11.38 years old, ranged from 28-75 years old, there is no significant difference between both groups regarding Age and sex. In our study there were 2 patients with stage I & 18 patients with stage II & 10 patients with stage III in Group (1) while there were 4 patients with stage I & 18 patients with stage II & 8 patients with stage III in Group (2). In our study there were only one patient who has downstaging in cases of cancer colon while in rectal cancer there were 7 patients dawnstage from T3 to T2 & 18 patients dawnstage from T2 to T1 & 4 patients dawnstage from T1 to T0. In our study there is statistically significant difference between group (A) & group (B) regarding Conversion rate as it is 30% of resection without neoadjuvant Vs 43.3% of resection with neoadjuvant this due to adhesions induced by neoadjuvant therapy & decreased experience of the surgeon & patients selection & intraoperative facilities . There is no difference between both groups regarding pre and post-operative complications .Complications after laparoscopic colorectal resection among the studied groups. Conversion rate, intraoperative bleeding, intraoperative ureteric injury and post-operative adhesions and post-operative Incisional hernia is found in (30%, 26.7%, 3.3%, 20%&13.3%) respectively in group (A) versus (43.3%, 30%, 6.7% ,23.3% &6.7%) respectively in group (B) the intraoperative complications were due to deceased surgeon's experience , extensive adhesions , disturbed anatomy, technical problems. In comparison to study made by **Gupta & Watson** the rate of conversion was 8% while literature states the rate of conversion 17-18% . laparoscopic colorectal resection using highly technical instruments (eg : high resolution camera) allows the surgeon to easily identify the gonadal vessels , ureters and this minimize their injuries **(5) .**In our study there is no statistically difference between both groups in Number of resected LN, operation time and amount of blood loss intraoperative, as regard the mean number of LN resected among patients of group (A) it is 13.63± 2.73, with a range from (8-18). While in group (B) mean number of LN resected is 14.96± 3.72, with a range from 8-22 LN resected. In comparison to other study, The least number of lymph nodes removed is reported as 12 for accurate staging. Our mean number of lymph nodes in pathology

report was 17, and all the resected specimens had free surgical margins **(6)& (7).** The operation time in group (A) ranging from 100-300 minutes with median 165 min, while in group (B) the operation time ranging from 110-185 minutes. The mean of hospital stay among group (A) is 5.63± 1.86, with a range from (2-8) days. While in group (B) mean of hospital stay is 5.8 ± 2.47, with a range from 1-9 days, with no statistical difference .The hospital stay in group (A) ranging from 2-8 days with median 6 days, while in group (B) the hospital stay ranging from 1-9 days. In our study there is no difference between both groups in number of deaths as 5 patients (16.7%) died in group (A) due to tumor recurrence with lung metastasis in 2 cases , anastomotic leakage in 3 case versus only one patient (3.3%) died in group (B) due to anastomotic leakage. Regarding need for reoperation there is statistically difference between both groups as 23.3% vs zero % of patients in group (A) versus group (B) respectively need for reoperation.In our study there were 25 out of 30 patients survived in group (A) while in group (B) there were 29 patient out of 30 survived, the over all death in both groups is 10%.By the end of the study there is difference in survival time distributions between both groups as mean duration of survival among group (A) is 15months with (C.I:14.3-15.6) 95% confidence interval, while in group (B) it is 16.75 months and (C.I:16.41-17.11), the overall survival is 15.9 months in the studied groups.

CONCLUSION

Laparoscopic colorectal resection after neoadjuvant chemo-radiotherapy has higher conversion rate & longer duration of surgery. Mortality & morbidity are equal in both groups but has the advantages of downstaging the cancer ,minimize locoregional recurrence , facilitate resection , improve overall & disease survival rate**.**

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Conflicts of interest

There are no conflicts of interest.

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