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Evaluation of Total Mesorectal Excision With or Without Lateral Pelvic Lymph Nodes Dissection for Middle and Lower Rectal Cancer

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ABSTRACT

Background: The most important prognostic factor in colorec-tal cancer is nodal status, and lymph node metastasis is a de-termining factor for adjuvant chemotherapy and subsequently key to predicting disease free and overall survival. **Methods:** A descriptive prospective study was conducted on 40 patients pre-senting with middle and low rectal cancer to the outpatient clinic of Menoufia University Hospitals. All patients in the study will require resection of their tumors by total mesorectal excision by open and laparoscopic techniques. Patients will be divided into 2 groups: Group A: was operated without lateral pelvic lymph nodes dissection. Group B: was operated with lateral pelvic lymph nodes dissection during the period between November 2018 and November 2020. **Results:** The main presentation of patients was bleeding per rectum 12 (30%), 12 (30%) patients have constipation. 28 patients with adenocarcinoma (70%) and 8 mucinous (20 %) and 4 (10%) with signet ring. Sixteen patients undergo Low ant resection (40%), 16 patients with AP. resection (40 %) and 8 patients with Intersphencteic resection (20%). Regarding intraoperative data, with a mean operative time was (90.00 ± 3.84 min.) for without Lateral pelvic L.N dissection and (122.91±4.89 min.) for with Lateral pelvic L.N dissection. **Conclusion:** Surgical mortality of LPLD is low, but there is an increase of morbidities in the form of prolonged operative time, intraoperative blood loss and genito-urinary malfunction. For avoiding the drawbacks of LPLD extended lymphadenectomies with sparing of the pelvic nerves is recommended. Lateral pelvic lymph node involvement is a regional disease that is curable. LPLD was effective to control recurrence at lateral nodes sites.

Keywords: Pelvic Lymph node dissection, Cancer Rectum, Tumor Staging, local recurrence.

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INTRODUCTION

Colorectal cancer incidence in the western world is 28%to 35% of the total colorectal cancer incidence, with 15 to 25/100,000 new patients per year for both men and women. The risk increases with age, with a median age of 70 years at the time of diagnosis; the associated mortality is between 4 and 10 per 100,000 per year[1].

The most important prognostic factor in colorectal cancer is nodal status, and lymph node metastasis is a determining factor for adjuvant chemotherapy and subsequently key to predicting disease free and overall survival [2].

Patients with lower rectal cancer have an increased risk of lateral lymph node (LLN) metastasis because the lower rectum drains both upwards through the superior rectal vessels and laterally along the middle rectal vessels and then to the internal iliac vessels. The rates of LLN metastasis in rectal cancer have been reported to range from 8.6% to 29% [3].

Based on this, pelvic sidewall dissection has become a standard procedure for lower rectal cancer in Japan, although it is rarely performed in other countries. One reason that pelvic sidewall dissection is not performed in other countries may be because positive LLN would represent systemic spread rather than regional disease [4].

Gilchrist first described the lymphatic spread of rectal neoplasms in 1938, and the term 'lateral lymph node' (LLN) was devised to encompass the common, external and internal iliac and obturator nodes in relation to rectal malignancies. The spread to these areas accounts for a significant proportion of the disease, with a reported incidence of 10–25 per cent [5].

Curative resection for colorectal cancer should include removal of the lymphatic drainage of the tumour bearing segment of bowel. The exact extent of the lymphadenectomy required for colorectal cancer, however, remains a matter of debate. [6]

The standardization of the technique of total mesorectal excision (TME) with accurate dissection of the anatomical plane enveloping the rectum and mesorectum constitutes major progress in rectal cancer surgery. TME has achieved much lower local recurrence rates [7].

Moreover, progress in chemoradiotherapy has achieved good local control and better survival rates in many Western countries. In Japan, rectal cancer with LLN involvement is considered a locally-advanced disease, and autonomic nerve-preserving LPND has now become a standard surgical treatment. However, LLN disease in Western countries is generally considered metastatic in nature, and patients are usually subject to neoadjuvant cheomoradiotherapy followed by total mesorectal excision (TME) surgery [8].

These studies have shaped the current Western practice of combining TME with chemo-radiation to achieve good oncological results for rectal cancer. Nevertheless, there are still cases of local recurrence, which is a significant clinical problem that is associated with severe morbidity, a low likelihood of salvage, and eventually death [9].

So, we Evaluated total mesorectal excision with or without lateral pelvic lymph nodes dissection for middle and lower rectal cancer on short term outcome.

Patients and Methods

A descriptive prospective study was conducted on 40 patients presenting with middle and low rectal cancer to the outpatient clinic of Menoufia University Hospitals. All patients in the study will require resection of their tumors by total mesorectal excision by open and laparoscopic techniques.

Patients will be divided into 2 groups: **Group A**: was operated without lateral pelvic lymph nodes dissection. **Group B**: was operated with lateral pelvic lymph nodes dissection during the period between November 2018 and November 2020.

Inclusion Criteria are Operable cases of middle and low rectal cancer by MRI and CT scan criteria which include no permeation of surrounding fat planes, no encasement of major vascular structures, no extensive local spread and no distant metastases or peritoneal infiltration will be

included in this study, Medically and anesthetically fit patients, All Tumor grades of differentiation, Patients after receiving neoadjuvant therapy for middle and low rectal cancer and Cases candidates for sphincter saving procedures.

Exclusion Criteria are upper rectal tumours, Tumor Stage IV with unresectable metastasis, previous pelvic lymphadenectomy for a disease other than rectal cancer, All cases with perforation or obstruction, Tumour recurrence and Irresectable lesion.

Preoperative preparation:

All patients were subjected to the following: Full history with history of neoadjuvant therapy, clinical examination and clinical staging, Complete laboratory investigations, Tumour markers including CEAand CA19-9, Complete radiological investigations (Abdominal CT, MRI pelvis, Endorectal ultrasound and colonoscopy). Informed consent was taken from all patients; Ethical approval was taken from the ethical committee of the hospital for all patients.

Surgical technique:

- Anesthesia: All procedures were performed under general anesthesia with endotracheal intubation.
- Position: Patient positioned supine with sacrum positioned over the table break or over a roll to allow for hyperextension and better vision into the pelvis.
- Incision: The abdomen is entered through an lower midline incision, Assisted Laparoscopic or Laparoscopic operation.
- Exploration: Careful inspection and palpation of the abdominal cavity, liver and pelvis was done, to exclude the evidence of disseminated disease.
- Total mesorectum exicision and Pelvic lymphadenectomy.

It was done for all patients:

Total mesorectal excision With or with out pelvic lymph node dissection

1. Lateral Pelvic Lymph node Dissection consists of a complete dissection of the endopelvic fascia together with the rectum, mesorectum, and all lymph nodes as well as the lymphatic cellular tissue medially to the common and internal iliac vessels. Clearance of the obturator region was performed preserving the obturator nerve, 2 ureters and the superior vesical artery.

2. The internal iliac vessels were exposed and dissected to uncover the root of the middle rectal artery and the middle rectal vein which are ligated and divided at their root.

3. After complete mobilization of the lateral aspect of the rectum, the lateral vesical and obturator spaces are opened between the internal iliac vessels and the pelvic side wall, and clearance of lateral lymphatic tissue in these spaces is carried out while preserving the obturator nerve and vessels and the visceral and parietal branches of the internal iliac vessels, such as the superior gluteal and the pudendal vessels.

- Low anterior resection, ultralow anterior resection, abdominoperineal resection or intersphicteric resection was done. Then refashioning of the route of the fecal passage: either by colo-anal anastomsis with temporary covering ileostomy (in intersphicteric and ultralow anterior resection). Or colo-rectal anastomosis with temporary covering ileostomy in low rectal carcinoma. Ileostomy was done when indicated.
- After careful hemostasis multiple drains were inserted for adequate drainage then Closure of the abdominal wall in layers. Closure of site of ports in laparoscopic surgery.

All patients were given triple antibiotics, and daily LMWH given regularly as a prophylaxis again DVT.

- All patients started oral within 2-4 postoperative days.

Statistical Analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS software (Statistical Package for the Social Sciences, version 21, SPSS Inc. USA). Data were described using mean and standard deviation (SD) and frequencies according to the type of the data

(quantative or categorical respectively). Pain scores at each time period were compared using the Mann-Whitney U test. Total number of analgesics, intraoperative fentanyl use and the time to first analgesia were analyzed using Student t-test. Categorical variables were compared using chi-square analysis or Fisher exact test. In all tests, data with a P < 0.05 were considered statistically significant. We used one way Anova test to compare between means of categorical and numerical data.

A P value less than 0.05 was considered statistically significant. A univariant analysis with non-linear correlation (cubic spline functions) was used to evaluate the shape of the relationship between the continuous variables and outcome.

Table 1: Distribution of the studied group regarding clinical Presentation:

Clinical presentation	**Lateral pelvic L.N dissection (n=40)**		**Chi-square**	**P value**
	Group A	**Group B**		
Bleeding per rectum	8 (40%)	4 (20%)	2.000	0.06
Constipation	4 (20%)	8 (40%)		
Marked weight loss	0 (0%)	4 (20%)		
Pain	8 (40%)	4 (20%)		

Table 2: Intraoperative Outcome among the studied groups.

	Lateral pelvic L.N dissection (n=40)				**U**	***P-value***
	Group A		**Group B**			
	Mean ± SD		Mean ± SD			
Operative time (min)	90.00 ± 3.84		122.91 ± 4.89		11.662	<0.001*
Hospital stays (day)	4.11 ±0.34		6.60 ±1.42		5.67	<0.001*
Intraoperative complication	**N**	**%**	**N**	**%**	**FET**	***P-value***
a. Hemorrhage.	**2**	**10%**	**3**	**15%**	**2.15**	**0.073**
b. Vascular injury: internal iliac vessels.	**0**	**0%**	**0**	**0%**		
c. Injury to the bladder, ureter or urethra.	**0**	**0%**	**1**	**5%**		
d. Injury of the intestine.	**0**	**0%**	**0**	**0%**		
e. Obturator nerve injury.	**0**	**0%**	**0**	**0%**		

FET: Fishers exact test U: Mann-Whitney test *significant

Table 3: Surgical curability and local recurrence of rectal cancer among the studied group.

	Lateral pelvic L.N (n=40)				FET	*P-value*
	Group A		Group B			
	N	%	N	%		
Surgical curability (n)						
R0	16	80	19	95	4.444	0.035*
R1	4	20	1	5		
Local recurrence						
No	17	85	19	95	6.12	0.018*
Yes	3	15	1	5		

FET: Fishers exact test *significant

Table 4: Showed the postoperative pathological results of the dissected L.Ns.

		Total no. = 20
Mesorectal L.Ns		
Positive LN	Mean± SD	6.5 ± 1.5
	Range	0 – 13
Total LN dissected	Mean ± SD	18 ± 3.4
	Range	6 – 33
Pelvic L.Ns		
Rt Side		
Positive LN	Mean ± SD	1.8 ± .4
	Range	0 – 2
Total LN dissected	Mean ± SD	4.3± 2.1
	Range	5 – 10
Lt Side		
Positive LN	Mean ± SD	2.5 ± .5
	Range	0 – 3
Total LN dissected	Mean ± SD	6 ± 1.8
	Range	5 – 10
Positive Pelvic L.Ns	Negative	16 (80.0%)
	Positive	4 (20.0%)

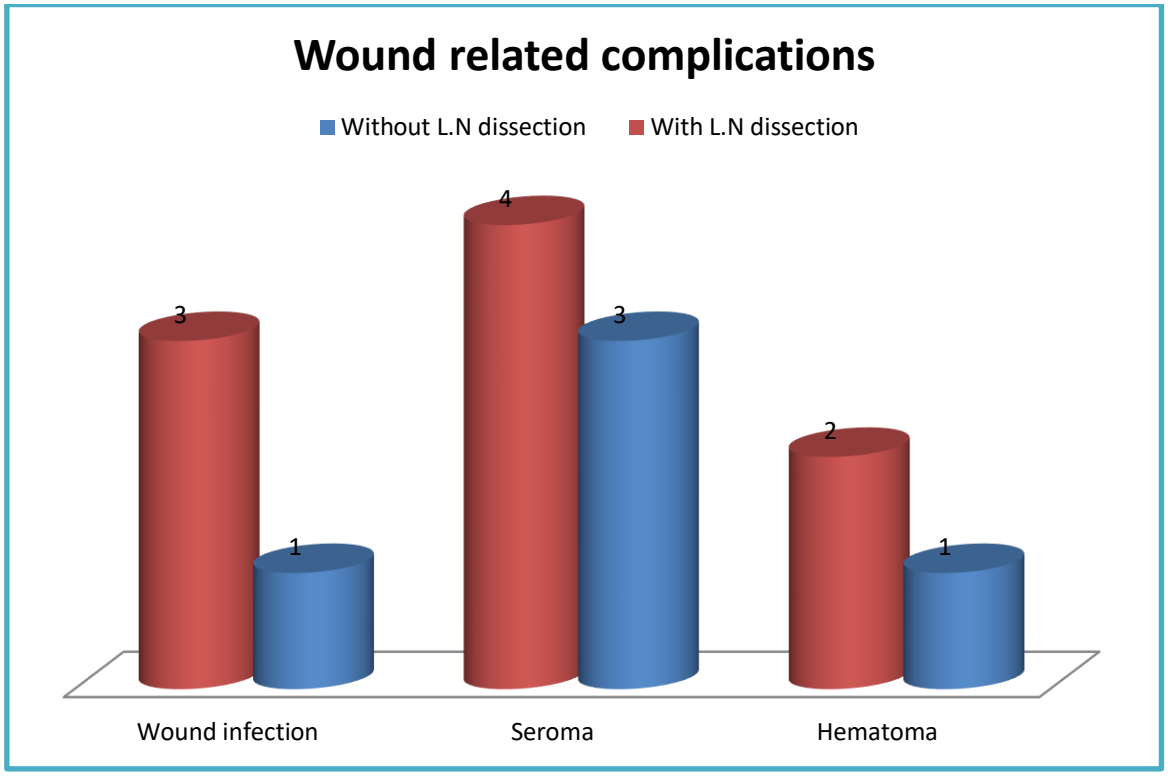

Figure 1: shows wound related complications in both groups.

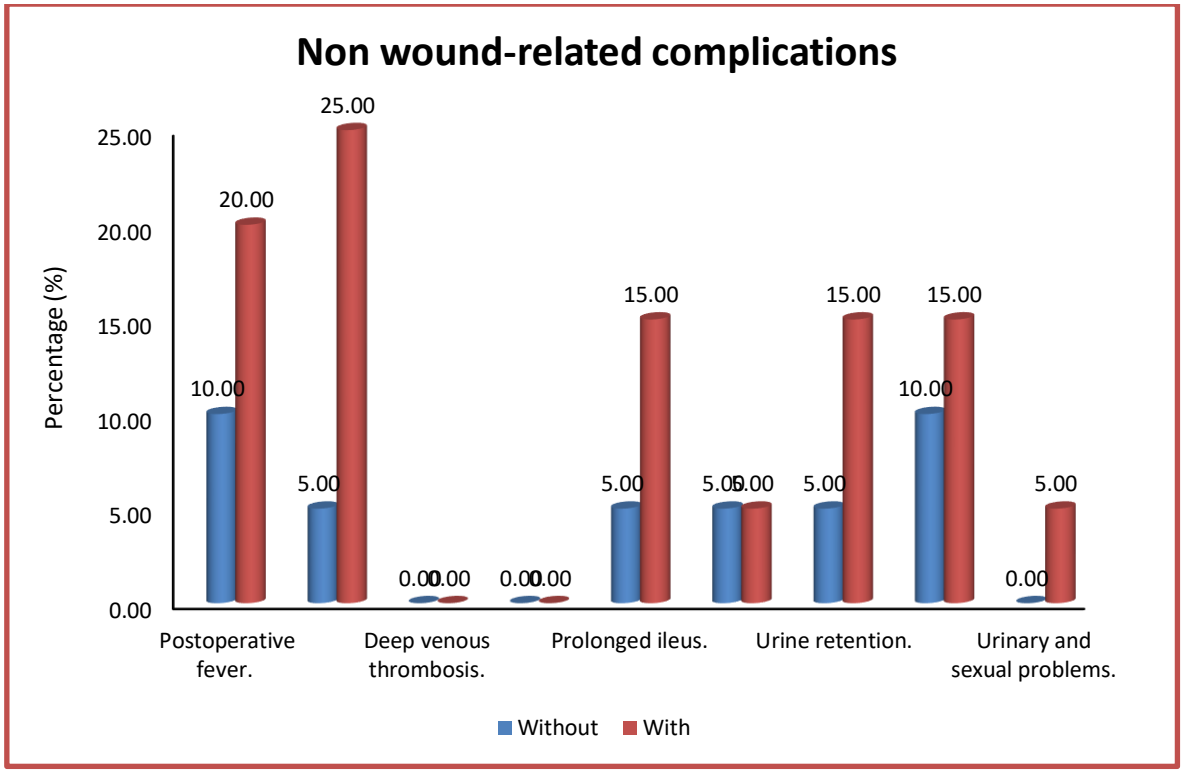

Figure 2: shows Non wound related complications in both groups.

RESULTS

Regarding patients characteristics, mean age of patients was 48.30 ± 10.78 years (range from 29–65). 24 patients were males and 16 patients were females, 12 were DM-HTN-Smoking. Among Group A, patients there were 12 male patients and 8 female patients and among Group B, patients there were 12 male patients and 8 female patients with no significant differences (P=.99). Group A, 12 of them have DM and

Group B, 12 of the have DM with no significant differences (P=.99).

The main presentation of patients was bleeding per rectum 12 (30%), 12 (30%) patients have constipation, 4 (10%) patients complaining of marked weight loss and 12 (30%) patients with lower abdominal pain.

Twelve patients presented with bleeding per rectum 4 of them in Group A and 8 of them in Group B. 12 patients presented with constipation 8 of them in Group A and 4 of them in Group B. 4 patients presented by marked weight loss, 4 of them in Group B. 12 patients presented by pain 4 of them in Group B and 8 of them in Group A (p=0.06).There was no significant difference between 2 groups regarding the clinical presentations.

Regarding pathology of rectal cancer among the studied group: 28 patients with adenocarcinoma (70%) and 8 mucinous (20 %) and 4 (10%) with signet ring, In Group A, 12 (60%) of the Adenocarcinoma, 4 (20%) of the Mucinous and. In Group B, 16 (80%) of the Adenocarcinoma, 4 (20%) of the Mucinous and 4 (20%) of the Signet ring, with no significant P-Value.

Seventeen patients undergo Low ant resection (40%), 16 patients with AP. resection (40 %) and 7 patients with Intersphencteic resection (17.5%). In Group A, 8 (40%) of the low ant resection, 9 (45%) of the AP. Resection and 3 (15%) of the Intersphencteic resection. Group B, 9 (45%) of the low ant resection, 7 (35%) of the AP. Resection and 4 (20%) of the Intersphencteic resection, with not comparable P-Value.

31 patients undergo open intervention (77.5%) and 9 patients with laparoscopic intervention (22.5 %). In Group A, 16 (80%) of the open and 4 (20%) of the lap. In Group B, 15 (75%) of the open and 5 (25%) of the lap, with no significant P-Value.

Regarding intraoperative data, with a mean operative time was (90.00 ± 3.84 min.) for Group A and (122.91±4.89 min.) for Group B.

Mean hospital stay was 4.11 ±0.34 and 6.60 ±1.42 days for Group A and Group B, respectively with a significant difference (p=0.029).

Regarding intraoperative complications, Haemorhage is more in group with pelvic L.N dissection (15%) than group without L.N dissection (10%) with insignificant difference (P= .1).

Regarding injury to bowel, and vascular injury (internal iliac vessels); no reported cases in both groups. The outcome between both groups is comparable with no significant difference expect for operative time and hospital stay.

We assessed post-operated complication, and categorized into wound related complication and not wound related complication. Hematoma, Seroma, Wound infection was higher in group B than group A with insignificant difference (P-value: .12, .18, .06; respectively).

Not wound related complications were assessed regarding Post-operative fever, and prolonged lymph drainage as higher in group B than another group A with significant P-value (.04, .02; respectively).

No reported cases of pulmonary embolism, DVT, or prolonged ileus. There was only one case of urinary and sexual problems (sexual desire decreased and in complete erection) in group B.

Regarding surgical curability (n) of rectal cancer among the studied group. 35 patients with R0 (87.5%) and 5 patients with R1 (12.5%) and 36 patients with no local recurrence of rectal cancer (90%) and 4 patients with local recurrence (10%). In Group A surgical curability (n), 16 (80%) of the R0 and 4 (20%) of the R1. Group B; surgical curability (n), 19 (95%) of the R0 and 1 (5%) of the R1, with significant P-Value. Group A; local recurrence, 17 (85%) of the No and 3 (15%) of the yes. In Group B; local recurrence, 19 (95%) of no local recurrence and 1 (5%) of local recurrence, with significant P-Value

Postoperative pathological results of the dissected lymph nodes were assessed. Mesorectal lymph nodes positivity range (from zero to 13) with Mean± SD (6.5 ± 1.5), and total mesorectal lymph nodes dissected range (from 6 to 33) with Mean± SD (18 ± 3.4).

DISCUSSION

The significance of rectal lymphatic drainage anatomy was discussed as a guide to proper excision of its malignancy. However, there are great variations in the application of these bases, such that the optimal management is still debatable, especially as regard the extension of lymphadenectomy [10].

Total mesorectal excision or mesorectal excision, in which at least a clear margin of 4 cm of the attached mesorectum distal to the tumor is resected, is the international standard surgical procedure for rectal cancer because it has a lower rate of associated local recurrence and higher rate of patient survival than conventional surgery .However, metastasis to lateral pelvic lymph nodes occasionally occurs in patients with clinical stage II or stage III lower rectal cancer, the lower margin of which is located at or below the peritoneal reflection. The incidence of lateral pelvic lymph node metastasis from lower rectal cancer is about 15%, and mesorectal excision with lateral lymph node dissection has been the standard procedure for patients with lower rectal cancer in Japan since it was introduced in the 1970s [11].

In the study by Matsumoto T, Ohue M, et al 2005 LPLND may be therapeutic in the presence of enlarged lateral pelvic nodes or may be prophylactic in the absence of any obviously enlarged lateral pelvic nodes. It is hypothesized that LPLND removes those nodes that contain micrometastasis and, hence, decreases the development of locoregional recurrence [12].

Our study was conducted on 40 patients with middle and low rectal cancer, 24 males and 16 females; with a mean age of 48.30 ± 10.78 years (range from 29–65 years). They were treated with total mesorectal excision with or without lateral pelvic lymphadenectomy. The main concern is to study the percentage of lateral pelvic lymph node involvement in middle and low rectal cancer and it's correlation with radiology; the number and groups of pelvic LN involved; and it's relation to site; grade and stage of the primary tumor and operative complications.

In our study; the most common presentation was bleeding per rectum (30%), followed by constipation (30%), then pain (10%), then weight loss (30%). *Moreno et al. (2016)* reported that the most frequent symptoms in series of 388 CRC patients between 2011 and 2014 included the following: bleeding per rectum (37 %), abdominal pain (34%), anemia (23%), change in bowel habits (1.3%) [13].

In our study CT and MRI reveals positive mesorectal L.Ns 12/20 (60%) and pelvic L.Ns 4/20 (20%). Preoperative radiological staging showed that 10 (50%) patients were stage 2 and 10 (50%) patients were stage 3. *Ishibe et al. (2016)* lateral pelvic lymph-node metastasis was diagnosed on preoperative MRI in 16 patients (19.9 %). The overall patient-based sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of MRI were 75, 69.1, 36.4, 92.2, and 70.2 %, respectively. When a cut-off value of 10 mm was used for diagnosis, the corresponding values were 43.8, 98.5, 87.5, 88.1, and 88.1 %, respectively. The mean diameter of metastatic nodes (14.7 mm) was significantly larger than that of negative nodes (5.7 mm; $P < 0.01$) [14].

Jhaveri et al. (2015) MRI is the modality of choice for staging rectal cancer to assist surgeons in obtaining negative surgical margins. MRI facilitates the accurate assessment of mesorectal fascia and the sphincter complex for surgical planning. Multiparametric MRI may also help in the prediction and estimation of response to treatment and in the detection of recurrent disease [15].

In the study by Akiyoshi T, Ueno M, et al 2014 recent meta-analysis of local staging by ERUS and MRI ,highlighted some difference among these modalities with regard to distinguishing T category. The sensitivity these modalities for detecting muscularis propria invasion (T1vs T2) was similar, but the specificity of ERUS was better. MRI tended to over stage patients with T1tumors conversely ,the specificity of all modalities was similar for assessing perirectal fat invasion (T3status)but ERUS was more sensitive . MRI

appeared to under stage T3 tumors compared to ERUS .It could be argued that ERUS, when feasible more appropriately distinguishes T1from T2 and T2 from T3 cancers [16].

In our study ERUS and MRI were performed to detect T and N stage of tumor and total number of lymph nodes pre and after neoadjuvant therapy then comparison between clinical stage and pathological stage to detect the effect of neoadjuvant on LN and tumor we found the neoadjuvant therapy lead to down staging and down shifting of T& N stage [17].

In the study by Kobayashi et al 2009 studied 1272 patients of low rectal cancer in which LPLND was done in 784 patients. The oncological outcomes were compared between those who had undergone LPLND with those who had not undergone LPLND and found that the two groups were comparable in terms of rates of local recurrence and five-year overall survival. However, it was found that involvement of lateral pelvic nodes was an independent poor prognostic factor and indicator of local recurrence [18].

In our study we found that 20 % was positive for malignant cells and there was significant benefit with extended lymph node dissection in terms of recurrence.

On exploration of our patients: 4 patients (10%) have lateral pelvic LN infiltration; 22 patients (55%) have positive mesorectal LNs; 4 patients (10%) have both mesorectal and lateral pelvic L.Ns metastases.

Ogura et al. (2017) LPLN metastasis was found in 26 patients (24.3 %) in the LPLND group (19). *Furuhata et al. (2015)* the mean number of harvested lateral pelvic lymph nodes was 16.9 (7–27), and five patients (27.8 %) had lymph node metastases [20].

The pathology among the studied group was adenocarcinoma 28/40 (70%). *Kobayashi et al. (2009)* showed that 117 out of 784 (14.9%) patients of rectal cancer had positive lateral pelvic lymph nodes. According to the depth of invasion, the incidence of positive lateral nodes was 5.4% in pT1, 8.2% in pT2, 16.5% in pT3, and 37.2% in pT4 [21].

Japanese Clinical Oncology Group (JCOG): has started a phase 3 randomized-controlled clinical trial comparing TME alone and TME LPLND for stage II/III rectal cancer with extra mesorectal nodes less than 1 cm in size on MRI to determine the role of prophylactic LPLND. The final results of this study may better define the role of prophylactic LPLND. However, those patients receiving neoadjuvant or adjuvant CRT are excluded. Hence, the value of radiotherapy, which might be an alternative to LPLND, will not be assessed [22].

Georgiou et al 2009 did a meta-analysis comparing extended lymph node dissection versus conventional rectal cancer surgery in which they included 5502 patients from one randomized, three prospective nonrandomized, and 14 retrospective case-control studies. They found that there was no significant benefit with extended lymph node dissection in terms of survival or recurrence although intraoperative blood loss, duration of hospital stay, and sexual and urinary dysfunctions were significantly higher with extended lymph node dissection. Hence, they concluded that extended lymphadenectomy does not confer a significant oncological advantage but increased complications. However, this was based on retrospective studies performed over a long period of time with significant heterogeneity between the groups [23].

Fujita et al. (2003) stated that the most common complication with LPLND wound infection followed by anastomotic leak then ileus [24]. *Fujita et al. (2012)* stated that the most common complication in patients submitted to TME + LPLND was urinary retention (18%) followed by anastomotic leak (18%) then infection with normal neutrophil count (16%), wound infection (10%) and pelvic abscess (2%) [25].

CONCULSION

The most common presentation of low rectal cancer is bleeding per rectum, followed by constipation and pain. The more tumor invasion, the

more likelihood of lateral pelvic nodal metastasis.

Surgical mortality of LPLD is low, but there is an increase of morbidities in the form of prolonged operative time, intraoperative blood loss and genito-urinary malfunction. For avoiding the drawbacks of LPLD extended lymphadenectomies with sparing of the pelvic nerves is recommended. Lateral pelvic lymph node involvement is a regional disease that is curable. LPLD was effective to control recurrence at lateral nodes sites.

DECLARATIONS

Conflict of interest: The authors declare that there is no conflict of interests.

Ethical approval: Ethical approval was granted for the study by Menoufia University-Faculty of Medicine`s ethics committee according to the Declaration of Helsinki. It was taken for research done on patients diagnosed with rectosigmoid neoplasm.

References:

1. Akiyoshi T, Matsueda K, Hiratsuka M, Unno T, Nagata J, Nagasaki T, Konishi T, Fujimoto Y, Nagayama S, Fukunaga Y, Ueno M. Indications for lateral pelvic lymph node dissection based on magnetic resonance imaging before and after preoperative chemoradiotherapy in patients with advanced low-rectal cancer. Annals of Surgical Oncology. 2015; 22(3):614-20.
2. Allison AS, Bloor C, Faux W, Arumugam P, Widdison A, Lloyd-Davies E, Maskell G. The angiographic anatomy of the small arteries and their collaterals in colorectal resections: some insights into anastomotic perfusion. Annals of surgery. 2010; 251(6):1092-7.)
3. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017; 66(4):683–91.
4. Beck DE, Roberts PL, Saclarides TJ, Senagore AJ, Stamos MJ, Wexner SD, editors. The ASCRS textbook of colon and rectal surgery. Springer Science & Business Media 2nd ed; New York, 2011.
5. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system, 4th edition. Lyon, France: International Agency for Research on Cancer 2010.
6. Brown G, Kirkham A, Williams GT, Bourne M, Radcliffe AG, Sayman J, Newell R, Sinnatamby C, Heald RJ. High-resolution MRI of the anatomy important in total mesorectal excision of the rectum. American journal of roentgenology. 2004; 182(2):431-9.
7. Butte JM, Tang P, Gonen M, et al. Rate of residual disease after complete endoscopic resection of malignant colonic polyp. Dis Colon Rectum 2012; 55:122-7.
8. Canessa CE, Badía F, Fierro S, Fiol V, Háyek G. Anatomic study of the lymph nodes of the mesorectum. Diseases of the colon & rectum. 2001; 44(9):1333-6.
9. Chen JS, Hsieh PS, Chiang JM, et al. Clinical outcome of signet ring cell carcinoma and mucinous adenocarcinoma of the colon. Chang Gung Med J 2010; 33:51-7.
10. Cheng J, Chen Y, Wang X, Wang J, Yan Z, Gong G, et al. Meta-analysis of prospective cohort studies of cigarette smoking and the incidence of colon and rectal cancers. Eur J Cancer Prev. 2015; 24(1):6–15.
11. Corman ML, et al. Corman' colon and rectal surgery. 6th rev ed. Philadelphia: Lippincott Williams and Wilkins, 2012.
12. Cress RD, Morris C, Ellison GL, Goodman MT. Secular changes in colorectal cancer incidence by subsite, stage at diagnosis, and race/ethnicity, 1992-2001. Cancer. 2006; 107(5):1142-1152.
13. Dayal S, Nick B, and Tom C. "Evolution of surgical treatment for rectal cancer: a review." Journal of Gastrointestinal Surgery 2017; 21(7): 1166-1173.
14. Dujovny N, Quiros RM, Saclarides TJ. Anorectal anatomy and embryology. Surg Oncol Clin N Am. 2014; 13:277–93.
15. Edwards BK, Ward E, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010; 116(3):544-573.
16. Fazio VW, et al. Current Therapy in Colon and Rectal Surgery E-Book. Elsevier Health Sciences, 2016.
17. Feldman D, Krishnan AV, Swami S, Giovannucci E, Feldman BJ. The role of vitamin D in reducing cancer risk and progression. Nat Rev Cancer. 2014; 14(5):342–57.
18. Ferlay J, Soerjomataram I, Ervik M. GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide: IARC cancer base no. 11. Lyon: International Agency for Research on Cancer; 2013.

19. Fields AC, et al. "Oncologic outcomes for low rectal adenocarcinoma following low anterior resection with coloanal anastomosis versus abdominoperineal resection: a National Cancer Database propensity matched analysis." International journal of colorectal disease 2019; 1-6.
20. Fleming M, et al. "Colorectal carcinoma: pathologic aspects." Journal of gastrointestinal oncology 2012; 3(3): 153.
21. Fleming M, et al. "Colorectal carcinoma: pathologic aspects." Journal of gastrointestinal oncology 2012; 3(3): 153.
22. Fujita S, Akasu T, Mizusawa J, Saito N, Kinugasa Y, Kanemitsu Y, Ohue M, Fujii S, Shiozawa M, Yamaguchi T, Moriya Y. Postoperative morbidity and mortality after mesorectal excision with and without lateral lymph node dissection for clinical stage II or stage III lower rectal cancer (JCOG0212): results from a multicentre, randomised controlled, non-inferiority trial. The Lancet Oncology. 2012; 13(6):616-21.
23. Fujita S, Mizusawa J, Kanemitsu Y, Ito M, KinugasaY, Komori K, et al. Mesorectal excision with or without lateral lymph node dissection for clinical stage II/ III lower rectal cancer (JCOG0212): a multicenter,randomized controlled, noninferiority trial. Ann Surg. 2017; 266(2):201–7.
24. Fujita S, Nakanisi Y, Taniguchi H, Yamamoto S, Akasu T, Moriya Y, Shimoda T. Cancer invasion to Auerbach's plexus is an important prognostic factor in patients with pT3-pT4 colorectal cancer. Diseases of the colon & rectum. 2003; 50(11):1860-6.
25. Fujita S, Yamamoto S, Akasu T. Risk factors of lateral pelvic lymph node metastasis in advanced rectal cancer. Int J Colorectal Dis. 2009; 24:1085–90.