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Correlation between Preoperative Radiological Finding of Pelvic Lymph Nodes in Rectal Cancer and Post-Operative Histopathology

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ABSTRACT

Background: In the surgical therapy of rectal cancer, the clinical and prognostic importance of the lateral pelvic lymph node (LPLN) compartment is still up for debate. The typical surgical treatment for rectal cancer is total mesorectal resection. MRI can be considered as a reliable tool to evaluate LPLN involvement, so surgery can extend to include lateral pelvic lymph node dissection (LPLND) in addition to the standard treatment.

Objectives: The aim of the current study was to correlate between preoperative radiological status of pelvic lymph nodes in rectal cancer and post-operative histopathology.

Methods: The study included 20 patients with middle and low rectal cancer with evident pelvic lymph node enlargement on preoperative MRI. All the included patients were subjected to surgical resection (either upfront surgery or after neoadjuvant therapy). Postoperative pathological data were analyzed and correlated to the preoperative radiological status of pelvic lymph nodes.

Results: The most common presentation was bleeding per rectum (50%) followed by pain (30%) then constipation (20%). The most common pathological type among study group was adenocarcinoma (80%) while mucinous carcinoma was encountered in (20%) of the patients. Postoperative pelvic lymph node involvement was found in 65% of the cases with a false positive rate of 35%. Their involvement was significantly related to increased depth of tumor invasion (T3 and T4) ($p=0.009$) with a significant longer hospital stay ($p<0.001$

Conclusions: Due to the increased likelihood of lateral lymph node involvement in T3-T4 lower rectal cancer patients, LPLND may be recommended.

Keywords: Cancer rectum, MRI of the rectum, Neoadjuvant chemotherapy, Pelvic dissection, Pelvic lymphadenectomy, Radiotherapy, Rectal adenocarcinoma.

INTRODUCTION

With 15 to 25 new cases of colorectal cancer per 100,000 new patients per year for both sexes, it is the third most prevalent disease in the world. With an associated mortality rate between 4 and 10 per 100,000 per year, it is the second leading cause of cancer deaths globally [1].

The presence of nodes in the mesorectum is the most crucial prognostic indicator for colorectal cancer. Adjuvant chemotherapy is determined by lymph node metastases, which also serves as a predictor of disease-free and overall survival [2].

The term "lateral pelvic lymph node" (LPLN) was developed to include the common, external, and internal iliac and obturator nodes in connection to rectal malignancies, with a reported incidence of 10–25%, and Gilchrist was the first to describe the lymphatic dissemination of rectal neoplasms in 1938 [3].

Because the lower rectum drains both laterally down the middle rectal arteries and upward through the superior rectal vessels before ending up in the internal iliac vessels, patients with lower rectal cancer are more likely to have LPLN metastases. From 8.6% to 29% of rectal cancer cases have been documented to have LPLN metastases [4].

Various combinations of surgery, radiation therapy, chemotherapy, and targeted therapy may be used as colorectal cancer treatments [5].

A significant advancement in rectal cancer surgery is the standardisation of the complete mesorectal excision (TME) approach with precise dissection of the anatomical plane around the rectum and mesorectum. TME has significantly reduced local recurrence rates [6].

The lymphatic drainage from the intestine segment that contains the tumour should be removed as part of the curative resection for colorectal cancer. But there is disagreement about the precise size of the lymphadenectomy needed for colorectal cancer [7].

In Japan, lateral pelvic lymph node dissection (LPLND), which preserves the autonomic nerve, is currently the go-to surgical procedure for treating rectal cancer that has spread to the lateral lymph nodes. However, LPLN illness is often treated with neoadjuvant chemoradiotherapy before TME surgery in western nations since it is commonly seen as a systemic spread disease rather than a local disease [8].

The most effective and precise tool for determining the condition of the circumferential resection margin and, consequently, the clinical outcome for rectal cancer, is magnetic resonance imaging (MRI). The centre of attention in the multidisciplinary team's therapy of rectal cancer is now accurate visualisation of the tumour, lymph nodes, and pelvic anatomy. Additionally, mesorectal and lateral nodal involvement can be assessed by MRI [9].

Imaging characteristics can be used to distinguish lymph nodes rather than only size criteria. Brown and colleagues found that an uneven shape and an inhomogeneous signal are the most accurate MRI criteria for lymph node metastases in their research of

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MRI with histologic correlation. So, predicting the preoperative status of LPLN may help in decision making for extending the lymph node dissection to include the LPLN whenever it is included as a routine step of surgical resection [10].

This study aimed to correlate between preoperative radiological finding of LPLN in rectal cancer and post-operative histopathology.

PATIENTS AND METHODS

A prospective study was conducted on 20 patients diagnosed to have rectal cancer who were candidates for resection of their tumors by total mesorectal excision and LPLND by open or laparoscopic approach. The study has been conducted at the Surgery Department, Faculty of Medicine, Menoufia University. The study has been conducted after ethical approval from the institute ethical and research committee. An informed consent has been obtained from all the patients to be included in the study.

Patient selection and preparation, the inclusion criteria were operable cases of middle and low rectal cancer with no distant metastases. All the included cases have enlarged LPLN on MRI. The included cases were either primary cases or after down staging with neoadjuvant therapy. Patients were selected to be medically and anesthetically fit for the operative procedure. However, patients with upper rectal or recurrent tumors, those with distant metastases, irresectability, or complications as obstruction or perforation were excluded from the study.

All the included patients were subjected to full history taking, thorough clinical examination, laboratory and radiological investigations required for diagnosis and staging of the disease including colonoscopy, biopsy and histopathological examination and pelvic MRI for assessment of tumor and lymph node status.

Surgical procedure

Endotracheal intubation was used under general anaesthesia for all procedures. The procedure was performed either by open or laparoscopic approach. Before proceeding for rectal dissection, abdominal exploration for disseminated disease was carefully performed. After high ligation of the inferior mesenteric artery, rectal dissection went distally to the levator ani muscle to accomplish entire mesorectal excision **(Figure 1),** and division of the proximal part of the sigmoid colon. Dissection proceeded with hypogastric nerve preservation **(Figure 2).** When the pelvic floor has been reached circumferentially around the rectum, low or ultralow anterior resection was performed whenever an adequate distal safety margin could be achieved, otherwise, the procedure proceeded to abdominoperineal resection.

The endopelvic fascia, rectum, mesorectum, all lymph nodes, and the lymphatic cellular tissue medially to the common and internal iliac arteries were completely dissected during LPLND **(Figure 3)**. The superior vesical artery and obturator nerve were preserved throughout the clearing of the obturator area. After achieving adequate hemostasis and inserting drains, closure was completed.

Assessment and evaluation, Surgical data as operative time, blood loss and transfusion requirement and intraoperative complications were recorded. Early postoperative findings as time to start oral feeding, time of drain removal and hospital stay including possible post operative complications were recorded. Quality of resection including circumferential and distal margin and positivity, laterality, number of lymph nodes were assessed. The patients have been scheduled for follow up for two years during which screening for local recurrence and/or distant metastases have been performed.

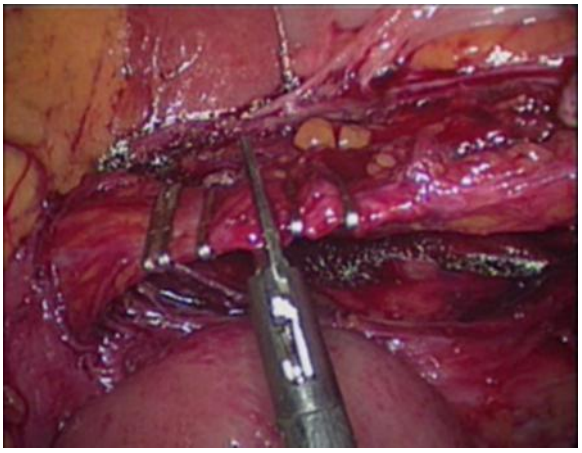

Fig (1): Cutting of IMA.
(Inferior mesenteric artery).

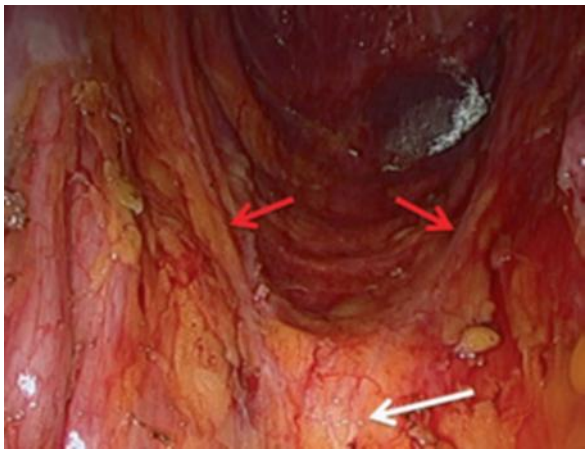

Fig (2): Hypogastric nerves (red arrows) and the superior hypogastric plexus (white arrow).

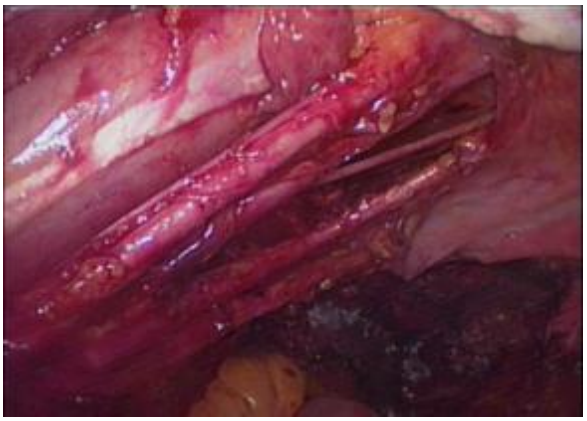

Fig (3): After Lap. lateral pelvic lymph node dissection showing IIA, EIA and obturator nerve.

Ethical considerations:

The Menoufia University Academic and Ethical Committee authorised the study. Each patient had to complete a written informed consent form in order to take part in the experiment. This study was guided by the World Medical Association's Helsinki Declaration, an ethical guideline for human research.

Statistical analysis

Data was gathered, tabulated, and statistically analyzed using SPSS version 26 on an IBM compatible laptop. A mean±standard deviation, or median (IQR) were used to provide quantitative data, while a number (N) and a percentage (%) were used to show qualitative data. Comparing quantitative variables between two sets of non-normally distributed data was done using Mann-Whitney's test (U).

To assess the relationship between qualitative variables, the Chi-square test (X^2) was applied. The likelihood of incorrectly rejecting the null hypothesis for a particular test is measured by the false positive ratio. Sensitivity is the likelihood that a sample will test positive if the patient has the condition, expressed as a percentage. Positive predictive value (PPV) is the likelihood that a subject's positive response is indeed positive.

RESULTS

During the period between November 2019 and July 2022, 20 patients with middle and low rectal cancer were enrolled in the study, **Table 1** shows the patients characteristics regarding age, gender, associated comorbidities, and family history. The main clinical presentation among the studied patient was bleeding per rectum by (50%) followed by pain (30%), then constipation (20%)**.**

Table (1): Demographic data and comorbidities

Parameters		**Total (No.= 20)**
Age (years)	Mean ± SD Range	51.5±9.55 36-67
Gender (No. %)	Females Males	6 (30%) 14 (70%)
Diabetes mellitus (No. %)	Negative Positive	8 (40%) 12 (60%)
Hypertension (No. %)	Negative Positive	8 (40%) 12 (60%)
Smoking (No. %)	Negative Positive	8 (40%) 12 (60%)
Family history (No. %)	Negative Positive	12 (60%) 8 (40%)

Table 2 shows the type of the performed operation for tumor resection where low and ultralow anterior resection were the most commonly used procedures. Only 3 patients developed complications, 2 (10%) patients had perineal wound and 1 (5%) had erectile dysfunction. Postoperative pathological reports revealed that adenocarcinomas represented the common pathology among studied patients by 80% (16 patients) while the remining 20% (4 patients) were mucinous type. Seventy percent of the resected tumors (14 cases) were moderately differentiated while 30% (6 cases) were poorly differentiated and none of the resected tumors was well differentiated.

Table (2): Operation type of rectal cancer among the studied patients

Operation type	Total no. = 20	
	No.	%
Low anterior resection	6	30.0%
Laparoscopic	3	15.0%
Open surgery	3	15.0%
Ultra-low anterior resection	6	30.0%
Inter sphincteric resection	4	20.0%
Abdominoperineal resection	4	20.0%
Laparoscopic	2	10.0%
Open surgery	2	10.0%

Table 3 shows the incidence of the tumor depth (T stage) of the resected rectal tumors where 55% (11 cases) were T3. The dissected LPLN were positive for metastases in 13 cases (65%) as shown in **Table 4.** Comparing this result with preoperative MRI there was 100% sensitivity, 35% false positive rate and positive predictive values (PPV) of 65%.

Table (3): (T) Stage of the resected rectal cancer

		Total (No. = 20)	
		No.	**%**
Stages	T1	0	0.0
	T2	5	25%
	Tз	11	55%
	T4	4	20%

Table (4): Preoperative MRI in relation to postoperative histopathology

Preoperative MRI	Postoperative pathology	
	Positive	**Negative**
Positive (No=20)	13 (65.0%)	7 (35.0%)
Right (n=12)	9 (75%)	3 (25%)
Left (n=8)	4 (50%)	4 (50%)
Bilateral (n=3)	3 (100%)	0 (0%)
Diagnostic value of MRI		
Sensitivity	100%	
False positive	35%	
Positive Predictive Value (PPV)	65%	

Table 5 shows the relation between different parameters and positive LPLND for metastases. It has been shown that positive lymph node metastases were significantly associated with bleeding per rectum and constipation (p=0.01), and with increased depth of tumor invasion (T3 and T4) (p=0.009). Lymph node positivity were significantly associated with longer hospital stay than negative cases (p<0.001). The included patients were followed up for two years during which no cases of local recurrence or distant metastases were encountered.

Table (5): Parameters associated with positive lateral pelvic lymph node positivity.

	Pelvic L.N				**Chi-square**	**P value**
	Positive N=13		**Negative N=7**			
	No	**%**	**No**	**%**		
Clinical presentation						
Constipation (n=4)	3	23	1	14.3	9.08	0.01*
Pain (n=6)	1	7.8	5	71.4		
Bleeding per rectum (n=10)	9	69.2	1	14.3		
Staging rectal tumor						
T2 (n=4)	0	0.0	4	57	9.29	0.009*
T3 (n=11)	9	69.2	2	28.7		
T4 (n=5)	4	30.8	1	14.3		
Outcome	Mean ± SD		Mean ± SD		**U**	***P-value***
Operative time (min)	146±17.12		140±27.48		0.586	0.102
Hospital stays (day)	7.6±1.42		5.0±0.84		3.81	<0.001*

U: Mann-Whitney test *Significant

DISCUSSION

Rectal lymphatic drainage anatomy has been considered important for more than a century as a guide for performing a good excision of its malignancy. However, there are significant differences in how these bases are used, therefore the best course of action is still up for debate, particularly with relation to the expansion of lymphadenectomy [11].

In the current study, bleeding per rectum was the most frequent clinical manifestation among the patients who were included, followed by discomfort and constipation. According to a research by **Högberg *et al.* [12],** the most common symptom was bleeding per rectum, which was then followed by anaemia and stomach discomfort, while the least common symptom was a change in bowel habits. In their investigation, **Jhaveri and Hosseini-Nik [13]** came to the conclusion that MRI is the preferred staging method for rectal cancer in order to help surgeons achieve negative surgical margins. For surgical planning, MRI makes it easier to accurately examine the mesorectal fascia and the sphincter complex. Additionally, multiparametric MRI may be used to predict and estimate therapy response and identify recurring illness. It could be argued that endo rectal ultrasound (ERUS), when feasible, can distinguish T1 from T2 and T2 from T3 cancers more appropriately.

However, **Delli *et al.* [**[14], in his study have concluded that rectal cancer can be staged accurately thanks to the high quality pictures of the whole mesorectum provided by pelvic MRI. Although it provides high resolution multiplanar noninvasive capabilities, the test is rather expensive. said that for staging of nodal involvement and locoregional tumour invasion in patients with rectal cancer, pelvic MRI is presently the gold standard.

As a result, it serves as the foundation for choosing whether to provide neoadjuvant chemoradiation. The most often employed parameter for predicting nodal metastasis is the greatest two-dimensional diameter. In the current study, ERUS was not performed as all the included cases within the study were selected to have radiologically positive LPLN. Instead, MRI has been performed to have an accurate assessment of the preoperative LPLN status [15]**.** In another study by **Jhaveri and Hosseini-Nik [13],** positive LPLN metastases were found in 27.8% of patients while the incidence was 24.3% in another study by **Dev *et al.* [16].** In the current study 65% of the included patients had LPLN infiltration that was proved pathologically.

This high incidence could be attributed to the selection criteria of the current study where only patients with radiologically positively pelvic lymph nodes have been included. However, cohorts included in other studies have selected to have rectal cancer regardless of the status of their pelvic nodes, consequently, a less percentage of positive pelvic lymph nodes have been detected. In the current study the sensitivity of MRI, false positive results and positive predictive value are 100%, 35%, 65% respectively.

The total 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, in a research by **Elsheekh *et al.*** [17].

In a study by **Kobayashi *et al.*** [18] involving 1272 patients with low rectal cancer, 784 of the patients underwent LPLND. When the oncological results of patients who had LPLND and those who had not were compared, it was discovered that the two groups had similar rates of local recurrence and five-year overall survival. Extended lymph node dissection and standard rectal cancer surgery were compared in a meta-analysis by **Georgiou *et al.*** [19], which comprised 5502 patients from one randomised, three prospective nonrandomized, and 14 retrospective case-control studies. They discovered that whereas intraoperative blood loss, hospital stay time, and sexual and urine dysfunctions were all considerably greater with extensive lymph node dissection, there was no discernible advantage in terms of survival or recurrence.

As a result, they came to the conclusion that protracted lymphadenectomy does not significantly improve oncological outcomes rather than decreasing them. But this was based on retrospective research done over a long period of time with a lot of variation in the groups. However, it was shown that LPLN involvement was a distinct poor prognostic factor and a sign of local recurrence [20].

In the current study, LPLND has been performed for all the 20 cases and patients have been followed up for two years postoperatively. Throughout the period of follow up, no local recurrence and/or distant metastases have been detected. This is considered a relatively short period to judge on local or distant relapse rate after pelvic lymphadenectomy, and at least five-year follow up has to be performed for accurate judgment of the effect of the procedure on relapse rate. It has been demonstrated that incidence of metastases to LPLN are directly related to the depth of the rectal tumors.

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, according to **Kobayashi *et al.*** [18]. Another research by **Sueda *et al.*** [21] established a clear correlation between the occurrence of lateral nodal involvement and abnormal T stage. The prevalence of lateral nodes was 7.1%, 17.9%, and 31.6% in pT2, pT3, and pT4, respectively. LPLN were infrequently present in pT1 tumours. This is consistent with the findings of the current study, which found that tumours larger than T2 were more likely to have pelvic lymph node involvement. Positive lateral nodes occurred 0/13 times in PT2, 9/13 times in PT3, and 4/13 times in PT4, respectively [21]. Most common detected postoperative complication in the current study was wound infection followed by erectile dysfunction. According to their findings [18, 21], anastomotic leak, ileus, and wound infection were the most typical complications associated with LPLND. According to **Fujita *et al.*** [22], urine retention (18%), anastomotic leak (18%), infection with a normal neutrophil count (16%), wound infection (10%), and pelvic abscess (2%), were the most frequent complications in patients who underwent TME and LPLND.

CONCLUSIONS

Pelvic sidewall dissection can be advised for patients with T3-T4 lower rectal tumours as they have the increased risk of positive lateral lymph nodes. MRI is an accurate predictor of pelvic lymph involvement. Broad spectrum antibiotic prophylaxis is mandatory to decrease the incidence of postoperative infection as it is the most commonly encountered complications.

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