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Original Article

Recurrent Rate in Rectal Cancer Patients with Clinically Suspected Lateral Pelvic Lymph Node Metastasis Following Neoadjuvant Chemoradiotherapy (CRT) and Total Mesorectal Excision (TME)

Thanachai Amornpetsathaporn, MD[1]
Kasidin Vitoopinyoparb, MD[1]
Siripong Sirikurnpiboon, MD[1]
Saraporn Kiattiubolwong, MD[1]
Ponprom Srisakorn, MD[2]

[1]*Division of Colorectal Surgery, Department of Surgery, Rajavithi Hospital, Bangkok, Thailand*
[2]*Department of Radiology, Rajavithi Hospital, Bangkok, Thailand*

Abstract

Background: The presence of lateral pelvic lymph node (LPLN) metastasis in rectal cancer has been associated with poor prognosis. We aimed to determine the recurrent outcome in patients with clinically suspected LPLN metastasis following neoadjuvant chemoradiotherapy (CRT) and total mesorectal excision (TME).

Materials and Methods: Rectal cancer patients who received neoadjuvant chemoradiotherapy (CRT) and total mesorectal excision (TME) between 2014 and 2023. The Patients' characteristics, LPLNs status, MRI or CT findings, operative and pathologic findings, recurrent rate, and survival rate were analyzed retrospectively.

Results: Among 131 patients, 88 were in the non-suspected group and 43 in the suspected group before CRT. After CRT, 86 patients in the non-suspected group remained non-suspected, while 2 developed newly suspected LPLN. In the suspected group, 15 patients responded to CRT, whereas 28 remained persistently suspected. The overall recurrence rate was 27.5% (36/131), including 4.6% (6/131) locoregional, 15.3% (20/131) distant, and 7.6% (10/131) both locoregional and distant recurrence.

In the non-suspected group, 25.6% (22/86) developed recurrence (local: 4.7%, distant: 16.3%, both: 4.7%), while both patients (100%) in the newly suspected group had recurrence involving both local and distant sites.

In the suspected group, there were responded group, 20% (3/15) had recurrence (distant: 13.3%, both: 6.7%), and in the persistently suspected group, 32.1% (9/28) had recurrence (local: 7.1%, distant: 14.3%, both: 10.7%).

The newly suspected group had significantly worse recurrence outcomes than the non-suspected group (HR = 8.95, 95% CI: 2.02–39.63; $p = 0.004$). However, there were no significant differences in recurrence rates for the responded group (HR = 1.11, $p = 0.865$) and persistently suspected group (HR = 1.23, $p = 0.607$) compared to the non-suspected group.

Post-treatment analysis revealed that LPLN location in the obturator region and unilateral involvement were significantly associated with increased locoregional recurrence risk. However, only 1 out of 16 patients with local recurrence developed lateral local recurrence.

Conclusion: Neoadjuvant chemoradiotherapy provided comparable local disease control between patients with and without clinically suspected LPLN metastasis in rectal cancer. The progression of LPLNs after CRT was a significant risk factor for recurrence compared to non-progression, highlighting the importance of post-treatment imaging in predicting oncologic outcomes.

Keywords: Lateral pelvic lymph nodes, Rectal cancer, Chemoradiotherapy, Total mesorectal excision

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Corresponding author: Kasidin Vitoopinyoparb, MD, Colorectal Surgery Division, Department of Surgery, Rajavithi Hospital, Bangkok 10400, Thailand; E-mail: Kasidinx@gmail.com

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Introduction

Although current treatments for locally advanced rectal cancer using chemoradiotherapy (CRT) followed by total mesorectal excision (TME) have significantly reduced the rate of local recurrence, with rates as low as 5.8–7.1%,[1-4] lymph node metastasis remains a crucial prognostic factor.[5] The theory suggests that lymph node spread in mid-to-low rectal cancer can extend laterally into the pelvic region.[6,7] Since TME surgery does not include the removal of these lateral pelvic lymph nodes (LPLN), residual cancer may remain. LPLNs involvement occurs in approximately 15–20% of patients with low-lying rectal cancer.[8] Numerous studies have indicated that such lateral lymphatic spread is a significant factor contributing to recurrence rates.[9-11]

There is a distinct difference in the treatment approaches for locally advanced rectal cancer. In Eastern regions, particularly Japan, the standard treatment involves TME with prophylactic lateral lymph node dissection (LLND) without CRT.[12-14] In contrast, in Western countries, the standard approach is CRT followed by TME without LLND[1,3,4,15] Several previous studies have suggested that both CRT combined with TME and TME combined with LLND can reduce recurrence rates with relatively comparable outcomes.[1,2,16,17] However, these methods are often insufficient to control lymph nodes in the lateral pelvic region, particularly in cases where LPLN metastasis is suspected.[9-11,16,17] It has been recommended to consider LLND selectively for patients with suspected LPLN involvement after preoperative radiation therapy, as this approach may yield the most optimal outcomes.[5,10,18-21]

It is well-known that LLND is a complex surgical procedure associated with a high rate of complications.[22-24] It is not yet widely adopted and is not currently a standard treatment recommendation. Additionally, there is no established international consensus on this matter due to differences in expertise and treatment environments,[25] underscoring the need to evaluate the advantages and disadvantages of LLND carefully. Factors such as the surgeon's experience and the risk of complications should be considered to determine the most appropriate approach for individual cases.

This study aims to clarify and evaluate the recurrence outcomes of rectal cancer patients with or without clinically suspected LPLN metastasis based on pretreatment imaging following neoadjuvant chemoradiotherapy (CRT) and total mesorectal excision (TME). The findings aim to provide insights into treatment efficacy and guide future management strategies for this high-risk patient population.

Materials and Methods

This retrospective study utilized single-center data from Rajavithi Hospital, Bangkok, Thailand, including rectal cancer patients treated with CRT followed by TME between January 2014 and December 2023. We included patients with mid-to-low rectal cancer, defined as tumors located within 10 cm of the anal verge (AV), with clinical staging of cT3/cT4 and/or node-positive disease. Patients who did not receive neoadjuvant CRT, those who underwent postoperative CRT, those with distant metastases at diagnosis, and individuals with a history of other malignancies were excluded.

Patients were categorized into two groups by suspicious lymph node based on pre-treatment imaging and further divided into four groups by lymph node responsiveness after post-treatment imaging, using criteria such as a short-axis lymph node size of ≥ 5 mm and morphological features,[26] including round shape, irregular borders, and mottled heterogeneity. All patients underwent neoadjuvant CRT, which included 50–50.4 Gy of radiation administered in 25–28 fractions with concurrent chemotherapy, followed by TME within 6–12 weeks after CRT. As mentioned above, post-CRT patients were classified into four groups based on post-treatment imaging findings: the non-suspected group, comprising patients who continued to show no malignant features after treatment; the newly suspected group, consisting of patients who developed new imaging features indicative of malignancy after CRT, despite having no concerning signs initially; the responded group, which included patients whose malignant features were controlled or reduced following CRT; and the persistently suspected group, involving patients whose malignant features remained unchanged on imaging, indicating persistent disease (Figure 1). Comprehensive demographic and clinicopathological data were collected, including age, sex, BMI, pre-operative CEA levels, tumor distance from the anus, pre-operative MRI findings, presence of EMVI, clinical and pathological staging, circumferential resection margin (CRM) involvement, and receipt of adjuvant chemotherapy.

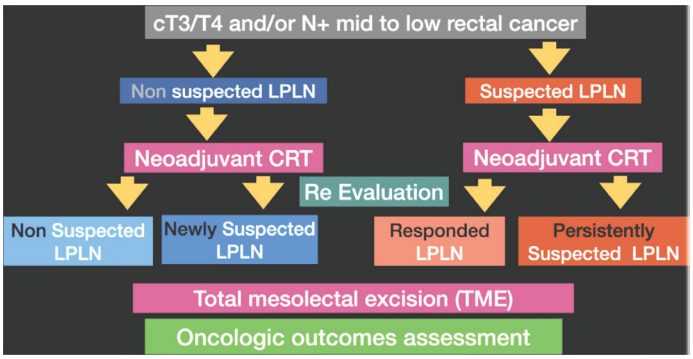

Figure 1

Our primary outcome is an overall recurrence, which refers to total tumor recurrence, including locoregional recurrence refers to the tumor recurrence within the pelvic cavity, further categorized into central and lateral recurrence based on the pelvic side wall; distant recurrence refers to tumor recurrence outside the pelvic cavity, involving distant organs or lymph nodes, Recurrence detection follows a defined protocol using computed tomography or colonoscopy findings, with the timing of recurrence measured from the date of surgery to the date of recurrence detection and recurrence-free survival (RFS) refers to the length of time after treatment during which a patient remains free from any signs or symptoms of cancer recurrence. Secondary outcomes focused on identifying specific LPLN factors, such as size, morphology, and location, that could influence the risk of locoregional recurrence in rectal cancer patients.

Statistical analysis was performed using SPSS version 29 (IBM Corporation, IL, USA). The chi-square or Fisher's exact test was used to analyze categorical data. The hazard ratio (HR) and 95% confidence interval were calculated. Where zeros caused problems with the computation of the hazard ratio, 0.5 was added to all cells. Binary logistic regression was utilized to ascertain the clinical variables linked to treatment failure, and a p-value < 0.05 was considered statistically significant.

Results

Out of a total of 131 patients who underwent CRT followed by TME, 43 patients had suspected LPLN on pre-treatment imaging, while the remaining 88 patients were categorized as non-suspected LPLN. After CRT, out of 88 patients in the non-suspected group, 86 remained non-suspected, while 2 developed newly suspected LPLN. Among the 43 suspected LPLN patients, 15 were classified as responded LPLN, and 28 as persistently suspected LPLN. Baseline characteristics are summarized in Table 1. The mean age was 57.7 ± 12.7 years in the suspected LPLN group, 60.33 ± 11.09 in the non-suspected group, 56.73 ± 12.23 in the responded group, and 58.25 ± 13.21 in the persistently suspected group. Male proportions were 62.8%, 60.2%, 46.7%, and 32.1%, respectively. Median pre-operative CEA levels were 4.22 in suspected LPLN, 5.01 in non-suspected, 4.53 in responded, and 3.47 in persistently suspected groups. The median tumor distance from the anus was 6 cm across all groups. Nearly half of the patients were evaluated by MRI: 47.7% in suspected, 46.5% in non-suspected, 46.7% in responded, and 46.4% in persistently suspected groups. Positive EMVI rates were 16.3%, 22.7%, 6.7%, and 21.4%, respectively. Most patients in all groups had clinical tumor stage cT3 (72.1% in suspected, 73.9% in non-suspected, 80% in responded, and 67.9% in persistently suspected groups). The operative approach was predominantly open or laparoscopic: 51.2% and 46.5% in suspected LPLN, 48.9% and 48.9% in non-suspected, 60% and 33.3% in responded, and 46.4% and 53.6% in persistently suspected groups. Most tumors were moderately differentiated, with rates of 74.4%, 61.4%, 73.3%, and 75% in suspected, non-suspected, responded, and persistently suspected LPLN groups, respectively. Pathological staging was predominantly ypT3 in all groups, while the pathological nodal stage was mostly ypN0: 58.1% in suspected, 65.9% in non-suspected, 53.3% in responded, and 60.7% in persistently suspected groups. Positive circumferential resection margins were low, observed in 2.3% of suspected LPLN, 5.7% of non-suspected, 6.7% of responded, and none in persistently suspected groups. A minority of patients did not receive adjuvant chemotherapy, with rates of 16.3%, 22.7%, 13.3%, and 17.9%, respectively.

Most characteristics showed no significant differences; however, ASA status was higher in persistently suspected LPLN compared to responded LPLN (p = 0.033), and clinical node stage cN2 was significantly higher in the suspected LPLN group (30.2%) compared to non-suspected LPLN (17.0%, p = 0.013), with no cN0 cases in the suspected LPLN group (Table 1).

Table 1 Demographic data

Characteristics	All patients n = 131 (100%)	Suspected LPLN n = 43 (32.8%)	Non-suspected LPLN n = 88 (67.2%)	*P*-value	Responded LPLN n = 15 (34.9%)	Persistently suspected LPLN n = 28 (65.1%)	*p*-value
Age (yr.)	59.4 (± 11.7)	57.7 (±12.7)	60.33 ± 11.09	0.242	56.73 (± 12.23)	58.25 (± 13.21)	0.715
Male (%)	80 (61.1)	27 (62.8)	53 (60.2)	0.778	7 (46.7)	9 (32.1)	0.348
BMI (kg/m²)	22.8 (± 4.1)	22.9 (± 4.2)	22.7 (± 4.1)	0.745	21.70 (± 4.09)	23.58 (± 4.15)	0.162
ASA (%)							
1	1 (0.8)	0 (0.0)	1 (1.1)		0	0	
2	69 (52.7)	25 (58.1)	45 (50.0)	0.708	12 (80)	13 (46.4)	0.033
3	59 (45.0)	18 (41.9)	41 (46.6)		3 (20)	15 (53.6)	
4	2 (1.5)	0 (0.0)	2 (2.3)		0	0	
Pre-operative CEA	4.6 (0.95-625.90)	4.22 (1.07-69.77)	5.01 (0.95-625.90)	0.296	4.53 (1.23-69.77)	3.47 (1.07-64.49)	0.665
Distance from anus (cm)	6 (0-10)	6 (1-10)	6 (0-10)	0.925	6 (1-10)	6 (1-10)	0.318
Pre-operative MRI (%)	62 (47.3)	42 (47.7)	20 (46.5)	0.896	7 (46.7)	13 (46.4)	0.988
EMVI Positive (%)	27 (20.6)	7 (16.3)	20 (22.7)	0.392	1 (6.7)	6 (21.4)	0.211
Post-treatment evaluation (wk)	7 (1-34)	7 (1-12)	7 (1-34)	0.253	8 (6-10)	7 (1-12)	0.186
Clinical staging							
cT -stage (%)				0.467			0.602
cT2	1 (0.8)	1 (2.3)	0 (0.0)		0	1 (3.6)	
cT3	96 (73.3)	31 (72.1)	65 (73.9)		12 (80)	19 (67.9)	
cT4	34 (26.0)	11 (25.6)	23 (26.1)		3 (20)	8 (28.6)	
cN-stage (%)				0.013			0.096
cN0	13 (9.9)	0 (0.0)	13 (14.8)		0	0	
cN1	90 (68.7)	30 (69.8)	60 (68.2)		13 (86.7)	17 (60.7)	
cN2	28 (21.4)	13 (30.2)	15 (17.0)		2 (13.3)	11 (39.3)	
Operative approach (%)				0.933			0.187
Open	65 (49.6)	22 (51.2)	43 (48.9)		9 (60)	13 (46.4)	
Lap	63 (48.1)	20 (46.5)	43 (48.9)		5 (33.3)	15 (53.6)	
Robotic	3 (2.3)	1 (2.3)	2 (2.3)		1 (6.7)	0	
Pathology							
Differentiation (%)				0.349			0.817
pCR	13 (9.9)	3 (7.0)	13 (14.8)		2 (13.3)	1 (3.6)	
Well	29 (22.1)	7 (16.3)	20 (22.7)		2 (13.3)	5 (17.9)	
Moderate	87 (66.4)	32 (74.4)	54 (61.4)		10 (73.3)	21 (75.0)	
Poor	2 (1.5)	1 (2.3)	1 (1.1)		0	1 (3.6)	
Pathological Staging							
ypT-stage (%)				0.666			0.572
ypT0	16 (12.2)	3 (7.0)	13 (14.8)		2 (13.3)	1 (3.6)	
ypT1	3 (2.3)	1 (2.3)	2 (23)		0	1 (2.3)	
ypT2	20 (15.3)	7 (16.3)	13 (14.8)		1 (6.7)	6 (21.4)	
ypT3	70 (53.4)	26 (60.5)	44 (50.0)		10 (66.7)	16 (57.1)	
ypT4	22 (16.8)	6 (14.0)	16 (18.2)		2 (13.3)	4 (14.3)	
ypN-stage (%)				0.685			0.672
ypN0	83 (63.4)	25 (58.1%)	58 (65.9)		8 (53.3)	17 (60.7)	
ypN1	29 (22.1)	11 (25.6)	18 (20.5)		5 (33.3)	6 (21.4)	
ypN2	19 (14.5)	7 (16.3)	12 (13.6)		2 (13.3)	5 (17.9)	
CRM positive	6 (4.6)	1 (2.3)	5 (5.7)	0.663	1 (6.7)	0	0.349
Adjuvant Chemotherapy (%)	104 (79.4)	36 (83.7)	68 (77.3)	0.392			
None	27 (20.6)	7 (16.3)	20 (22.7)	0.400	2 (13.3)	5 (17.9)	0.801
5FU	21 (16)	4 (9.3)	17 (19.3)		1 (6.7)	3 (10.7)	
Cape	11 (8.4)	5 (11.6)	6 (6.8)		1 (6.7)	4 (14.3)	
FOLFOX	38 (29)	15 (34.9)	23 (26.1)		4 (14.3)	10 (35.7)	
CapeOX	34 (26)	12 (27.9)	22 (25.0)		6 (40.0)	6 (21.4)	

Mean ± SD; Median (min-max); N (%)

Recurrence outcome

The overall recurrence rate was 27.5% (36 out of 131 patients), comprising 6 cases (4.6%) of locoregional recurrence, 20 cases (15.3%) of distant recurrence, and 10 cases (7.6%) of both locoregional and distant recurrence. Group-specific analysis revealed that in the non-suspected LPLN group, the overall recurrence rate was 25.6% (22 patients), with 4 cases (4.7%) of locoregional recurrence, 14 cases (16.3%) of distant recurrence, and 4 cases (4.7%) of both types. In the newly suspected LPLN group, the overall recurrence rate was 100% (2 patients), with both experiencing both locoregional and distant recurrences. For the responded LPLN group, the overall recurrence rate was 20% (3 patients), including 2 cases (13.3%) of distant recurrence and 1 case (6.7%) of both types of recurrence. In the persistently suspected LPLN group, the overall recurrence rate was 32.1% (9 patients), with 2 cases (7.1%) of locoregional recurrence, 4 cases (14.3%) of distant recurrence, and 3 cases (10.7%) of both locoregional and distant recurrence (Table 2).

Table 2 Recurrent rate between groups

Pre-CRT	Non-suspected LPLN n = 88 (%)		Suspected LPLN n = 43 (%)		All n = 131
Post-CRT	Non-suspected LPLN n = 86	Newly suspected LPLN n = 2	Responded LPLN n = 15	Persistently suspected LPLN n = 28	
All (%)	22 (25.6)	2 (100)	3 (20)	9 (32.1)	36 (27.5)
Locoregional (%)	4 (4.7)	0	0	2 (7.1)	6 (4.6)
Distant (%)	14 (16.3)	0	2 (13.3)	4 (14.3)	20 (15.3)
Both (%)	4 (4.7)	2 (100)	1 (6.7)	3 (10.7)	10 (7.6)

Recurrent rate n (%), CRT-Neoadjuvant chemoradiation, LPLN-Lateral pelvic lymph node

During the follow-up period, at 1 year, the recurrence rate was 5% in the non-suspected LPLN group, 50% in the newly suspected LPLN group, 9.1% in the responded LPLN group, and 19.6% in the persistently suspected LPLN group. By 2 years, recurrence rates increased to 9.1% in the non-suspected LPLN group, 100% in the newly suspected LPLN group, 27.3% in the responded LPLN group, and 41% in the persistently suspected LPLN group. Notably, in the newly suspected LPLN group, both cases experienced recurrence within 2 years, involving both locoregional and distant sites. Overall, recurrence rates were higher in patients with suspected LPLNs, with persistently suspected LPLNs showing a higher recurrence rate compared to responded LPLNs.

Survival analysis revealed that the recurrence rate in the newly suspected LPLN group was significantly worse, with a hazard ratio (HR) of 8.95 (95% CI: 2.02–39.63, $p = 0.004$). In contrast, the responded LPLN group showed an HR of 1.11 (95% CI: 0.33–3.74, $p = 0.865$), and the persistently suspected LPLN group had an HR of 1.23 (95% CI: 0.56–2.67, $p = 0.607$), indicating no significant differences in recurrence rates when compared to the non-suspected LPLN group (Figure 2).

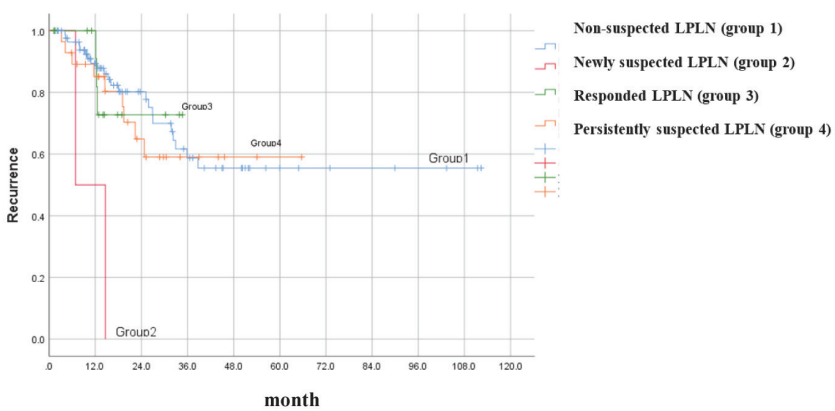

Figure 2 Survival analysis for recurrence

Univariate analysis evaluating LPLN factors affecting recurrence revealed that pre-treatment factors such as size, location, and side did not significantly influence recurrence risk. However, post-treatment analysis indicated that the location of LPLNs in the obturator region and unilateral involvement were significantly associated with an increased risk of locoregional recurrence (Table 3).

Table 3 Univariate analysis evaluating LPLN factors affecting recurrence

LPLN factors	Number of patients	Overall recurrence	N (%)	Locoregional recurrence	Distant recurrence
Pre-treatment					
Size and Morphology					
Non-suspected	88	1	24 (27.3)	1	1
Suspected	43	0.91 (0.45-1.82), 0.785	12 (27.9)	1.31 (0.47-3.61), 0.605	1.08 (0.50-2.31), 0.845
Location					
None	88	1	24 (27.3)	1	1
Internal iliac	13	1.16 (0.40-3.34), 0.788	4 (30.8)	1.37 (0.30-6.29), 0.683	1.02 (0.30-3.45), 0.972
Obturator	27	1.08 (0.47-2.52), 0.850	7 (25.9)	1.48 (0.46-4.75), 0.508	1.08 (0.43-2.71), 0.862
Both	3	1.02 (0.14-7.52), 0.987	1 (33.3)	NA	1.25 (0.17-9.30), 0.830
Side					
None	88	1	24 (27.3)	1	1
Unilateral	38	1.13 (0.55-2.31), 0.742	10 (26.3)	1.46 (0.53-4.03), 0.465	1.09 (0.49-2.39), 0.838
Bilateral	5	0.87 (0.12-6.49), 0.896	2 (40)	NA	1.02 (0.14-7.62), 0.985
Post-treatment					
Size and Morphology					
Non-suspected	101	1	25 (24.7)	1	1
Suspected	30	1.44 (0.71-2.92), 0.318	11 (36.7)	2.47 (0.92-6.64), 0.073	1.38 (0.63-3.02), 0.418
Location					
None	101	1	25 (24.7)	1	1
Internal iliac	10	1.68 (0.58-4.87), 0.335	4 (40)	2.22 (0.48-10.32), 0.309	1.50 (0.44-5.05), 0.516
Obturator	18	1.54 (0.63-3.78), 0.344	6 (33.3)	3.35 (1.12-10.03), 0.031	1.52 (0.57-4.05), 0.405
Both	2	1.23 (0.17-9.11), 0.840	1 (50)	NA	1.51 (0.20-11.28), 0.688
Side					
None	101	1	25 (24.7)	1	1
Unilateral	28	1.52 (0.73-3.16), 0.266	11 (39.3)	2.87 (1.06-7.71), 0.037	1.43 (0.63-3.23), 0.389
Bilateral	2	0.95 (0.13-6.91), 0.947	0 (0)	NA	1.08 (0.15-8.08), 0.937

Hazard ratio HR (95% CI), *p*-value
NA - not applicable

Our study's univariate analysis identified age < 50 years, EMVI, pT stage (especially pT4), CRM involvement, and pathologic node positivity as factors associated with recurrence. However, multivariate analysis revealed that only pathologic nodal staging remained an independent predictor of recurrence (Appendix 1).

Discussion

Our study found a recurrence rate of approximately 27.5%, with locoregional recurrence at 12.2% and distant recurrence at 22.9%. This differs from the study by Beck et al., which reported an overall recurrence rate of 52.9%, locoregional recurrence of 17.9%, and distant recurrence

of 35.6%. Notably, in that study, only 45.8% of patients received both CRT and adjuvant therapy, with more than half undergoing surgery alone.[27] CRT plays a crucial role in reducing locoregional recurrence by downstaging the tumor and improving local control. In contrast, adjuvant chemotherapy helps decrease systemic recurrence by targeting micrometastases that may not be eradicated by local treatment alone. Notably, distant recurrence was higher than locoregional recurrence, which may be attributed to the fact that 20.6% of patients in this study did not receive adjuvant chemotherapy (Table 1), potentially impacting the systemic recurrence rate.

When examining locoregional recurrence rates in each group, our study found rates of 9.4% in the non-suspected LPLN group, 6.7% in the responded LPLN group, and 17.8% in the persistently suspected LPLN group. In comparison, the newly suspected group had a 100% recurrence rate (Table 2). These findings are comparable to those reported by Ogura et al., who reported locoregional recurrence rates of approximately 10% in patients with no visible or non-suspected LPLNs and around 20% in the suspected LPLN group.[10] However, their study did not specifically address LPLN progression after CRT. In contrast, our study highlights that patients who developed newly suspected LPLNs after preoperative CRT had a significantly higher recurrence risk compared to both the non-suspected and clinically suspected LPLN groups, regardless of their response to CRT. This underscores the critical role of post-CRT imaging in identifying high-risk patients who may benefit from more aggressive treatment strategies. Additionally, this suggests that radiation may help control the lateral pelvic compartment, given the technology now available to cover the lateral pelvis,[28] while the disease in the newly suspected LPLN group appears to be more aggressive and less responsive to CRT. Additionally, a lack of precise tools to assess LPLN metastasis prior to treatment may contribute to variability in the definition of reactive versus pathologic LNs,[29] as different studies use varying cutoff sizes. Even within radiology-specific studies like the MERCURRY study,[30] there is still no clear consensus. The high recurrence rates in the newly suspected LPLN group may be due to some patients having LPLN that were either undetectable or smaller than the cutoff size before CRT, leading to false negatives. Following CRT, these LPLNs may progress, indicating that lateral pelvic disease persists despite treatment. For instance, two patients had a progression of disease after CRT, with one presenting a 4 mm obturator LPLN without malignant features and the other with an LPLN that increased from undetectable to 10 mm with malignant features post-CRT, though neither developed lateral local recurrence, with all recurrences being central. This differs from previous studies, which did not address the relationship between newly suspected LPLN and recurrence or poor prognosis, and provides new information that may warrant more careful consideration for this patient group.

In this study, locoregional recurrence occurred in 16 patients (12.2%), with only one case (6%) of lateral local recurrence, which was in the persistently suspected LPLN group. The patient had an extremely large LPLN of 18 mm pre-treatment, which decreased to 13 mm post-radiation. When compared with Kim et al.'s 2008 study, which found a 7.9% locoregional recurrence rate after CRT followed by TME, with lateral local recurrence making up 82.7% of cases, the difference might be explained by current radiation techniques covering the lateral pelvis. Furthermore, in the study by Kim et al., 87.5% of patients with lateral local recurrence had LPLNs larger than 10 mm, whereas only 4.3% had LPLNs smaller than 5 mm.[9] Our study indicates that unilateral involvement and obturator location are significant factors associated with higher rates of locoregional recurrence, a finding supported by the research of Kim et al. Their study demonstrated that irradiated patients with LPN metastasis had outcomes comparable to those with mesorectal node metastasis. Specifically, metastasis in internal iliac LPNs was similar to perirectal node metastasis, while metastasis in external LPLNs, including the obturator group, was analogous to intermediate LN metastasis.[31]

The limitations of our study include its retrospective design, small sample size, short follow-up period, and the fact that some patient data was collected during the COVID-19 pandemic, which may have influenced patient follow-up and the appropriateness of some treatments.

Conclusion

In conclusion, this study demonstrates that the recurrence rate of rectal cancer remains substantial, strongly influenced by the LPLN response to CRT. While locoregional recurrence was relatively low in non-progression groups, newly suspected LPLN cases showed a dramati-

cally higher risk. LPLN progression after CRT is a key predictor of recurrence, emphasizing the critical role of post-treatment imaging in risk assessment and treatment planning.

Conflict of Interest

The authors declare that there is no conflict of interest.

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None

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Appendix 1 Univariate and multivariate analysis for recurrence

Variable	Number of patients	Univariate HR (95% CI)	*p*-value	Multivariate HR (95% CI)	*p*-value
Age (y)					
≥ 50	108	Ref.			
< 50	23	2.24 (1.07, 4.65)	0.031	1.34 (0.55, 3.28)	0.522
Gender					
Female	51	Ref.			
Male	80	0.87 (0.44, 1.70)	0.676		
CEA					
≤ 5	68	Ref.			
> 5	63	1.12 (0.58, 2.16)	0.731		
ASA					
1,2	70	Ref.			
3,4	61	0.90 (0.46, 1.75)	0.759		
Tumor Location					
Mid, < 5 cm	70	Ref.			
Low, ≤ 5 cm	61	1.36 (0.71, 2.62)	0.354		
cT stage					
cT3	96	Ref.			
cT4	34	2.02 (0.99, 4.14)	0.053	0.98 (0.30, 3.21)	0.975
EMVI					
No	104	Ref.			
Yes	27	2.69 (1.34, 5.40)	0.006	1.39 (0.53, 3.61)	0.502
cN stage					
cN0	13	Ref.			
cN1	90	1.66 (0.39, 7.06)	0.492		
cN2	28	3.52 (0.78, 15.94)	0.103		
pT stage					
pT0	16	Ref.			
pT1,2	23	1.67 (0.17, 16.10)	0.655	1.46 (0.14, 14.62)	0.749
pT3	70	4.56 (0.61, 33.98)	0.138	2.45 (0.30, 19.72)	0.399
pT4	22	8.97 (1.16, 69.50)	0.036	3.00 (0.30, 30.46)	0.353
CRM					
Negative	125	Ref.			
Positive	6	3.04 (1.07, 8.62)	0.037	1.77 (0.45, 6.90)	0.411
pN stage					
pN0	83	Ref.			
pN1	29	0.22 (0.09, 0.51)	< 0.01	3.37 (1.43, 7.94)	0.006
pN2	19	0.99 (0.46, 2.16)	0.995	3.33 (1.27, 8.77)	0.015
Adjuvant Chemotherapy					
No	27	Ref.			
Yes	104	1.51 (0.46, 4.98)	0.497		

Ref. – Reference