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Lateral pelvic lymph node dissection based on nodal response to neoadjuvant chemoradiotherapy in mid/low rectal cancer: a retrospective comparative cohort study

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Purpose: Total mesorectal excision (TME) without lateral pelvic lymph node (LPN) dissection (LPND) is feasible in patients with mid/low rectal cancer showing a reduction in LPN size to ≤5 mm following neoadjuvant chemoradiotherapy (nCRT). We aimed to evaluate the clinical outcomes of selective LPNDs based on these criteria.
Methods: Patients with mid/low rectal cancer and LPNs >5 mm before nCRT were included and classified based on nCRT response (post-nCRT LPN size ≤5 mm [responsive] *vs.* >5 mm [persistent]) and surgical procedure (TME alone *vs.* TME + LPND). In the responsive group, LPND was selectively performed only if morphologic predictors of LPN metastasis were present. Clinical outcomes were analyzed across subgroups.
Results: Of 122 patients, 82 were in the responsive group. Within this group, 61 underwent TME alone and 21 underwent TME + LPND. No locoregional recurrence was observed in either subgroup of the responsive group, with similar systemic metastasis rates (13.1% *vs.* 14.3%, $P > 0.99$). The TME alone subgroup showed significantly smaller post-nCRT LPN sizes (1.7 ± 2.1 mm *vs.* 3.9 ± 1.8 mm, $P < 0.001$) and lower ycN positivity rates (31.1% *vs.* 71.4%, $P = 0.001$).
Conclusion: Selective LPND based on post-nCRT LPN size ≤5 mm and the absence of morphologic predictors of metastasis may serve as a feasible option for managing mid/low rectal cancer with enlarged LPNs, thereby optimizing local control and reducing unnecessary surgeries.
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Key Words: Local neoplasm recurrence, Lymph node dissection, Lymphatic metastasis, Neoadjuvant therapy, Rectal neoplasms

INTRODUCTION

Neoadjuvant chemoradiotherapy (nCRT) followed by total mesorectal excision (TME) is the standard treatment for patients with locally advanced mid/low rectal cancer [1-5]. Although the incidence of locoregional recurrence (LR) has been reduced with the introduction of nCRT, it remains at 5%–10% when nCRT is followed by TME [2,6]. LR of rectal cancer is a critical issue because it is associated with considerable morbidity and high mortality [7-9]. LRs following nCRT and TME predominantly recur in lateral pelvic lymph nodes (LPNs) with 60%–80% of all LRs [10,11]. Furthermore, approximately 40% of patients with recurrence in LPNs show no other local or distant metastasis [12-14].

Based on these findings, various studies have reported on the indications for LPN dissection (LPND) in patients with

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metastatic LPNs. Ogura et al. [15] reported that TME with LPND resulted in a lower 5-year lateral LR rate compared with that of TME alone when the short-axis (SA) diameter of the LPN was >7 mm on pretreatment MRI. Furthermore, several studies have reported an increased lateral LR rate in patients who did not undergo LPND after nCRT when they have an enlarged LPN on primary MRI, showing a linear relationship between nodal size and lateral LR [10,12,16,17]. However, because of concerns about operative morbidity and long-term sexual and urinary dysfunction associated with LPND [18,19], selecting patient groups for LPND more accurately without compromising oncologic outcomes is needed. The appropriate selection of candidates for LPND can be achieved through a multidisciplinary MRI-directed approach in patients with rectal cancer who undergo total neoadjuvant therapy [20]. In this prior study, LPND was more likely to be performed when the posttreatment SA diameter of LPNs exceeded 5 mm, demonstrating comparable oncologic outcomes.

Oh et al. [21] reported the pathologic and oncologic outcomes of LPND according to the nCRT response, assuming nCRT may affect LPND indications in patients with suspected LPN metastasis. In their study, there was no LPN metastasis in patients with responsive LPN (post-nCRT SA diameter ≤5 mm) who underwent TME with LPND after nCRT. Moreover, the LPN size after nCRT was a risk factor for lymph node metastases, and the persistent group (post-nCRT SA diameter >5 mm) had worse oncologic outcomes than the responsive group. The authors suggested that the decision to perform LPND should be based on the response of LPNs to nCRT.

Lacking a clear consensus on LPND indications, this study aimed to determine surgicopathological and oncologic outcomes of performing LPND in mid/low rectal cancer patients with metastatic LPNs, based on nodal response to nCRT and to evaluate whether this strategy is a feasible surgical option.

METHODS

Ethics statement

This study was performed according to the Helsinki Declaration and was approved by the Institutional Review Board of Seoul National University Bundang Hospital (No. B-2303-819-105). The requirement for informed consent was waived due to the retrospective nature of this study.

Study design and patients

This retrospective cohort study included patients with mid/low rectal cancer who underwent nCRT followed by TME with or without LPND for clinically suspected LPN metastasis between January 2012 and December 2022 at a single center. Patients were identified through a comprehensive review of electronic medical records using specific diagnostic codes for mid/low rectal cancer and procedure codes for nCRT and TME. The inclusion criteria were (1) histologically confirmed adenocarcinoma of the middle or distal rectum (<10 cm superior to the anal verge), (2) locally advanced disease stage (cT3 or cN+ based on CT or MRI), (3) SA diameter of LPN ≥5 mm on pretreatment MRI, (4) no distant metastasis in staging workup, (5) completion of the entire nCRT course, (6) no previous or concurrent malignancy, and (7) available surgical record and pathology report. Patients who received radiotherapy on the pelvis had hereditary colorectal cancer, underwent emergency surgery, or underwent transanal local excision were excluded.

Patients were classified into 2 groups based on the nodal response to nCRT. Those with an LPN size of ≤5 mm or >5 mm in the SA diameter on post-nCRT MRI were placed in the "responsive" and "persistent" groups, respectively. Both responsive and persistent groups were further subdivided into a group with TME alone and another that underwent TME with LPND.

Treatment details

Before undergoing nCRT, all patients received a rectal examination, colonoscopy, and abdominopelvic CT and MRI for staging workups. MR images were reviewed by 3 radiologists, each with over 10 years of experience. Radiologic evaluation of LPNs was conducted both before and after nCRT using pelvic MRI scans. LPNs were identified as lymph nodes located in the obturator, internal iliac, and external iliac regions. The transverse SA diameter of the largest LPN measured on MRI was used as the representative value. Clinically suspected LPN metastasis was defined as an SA diameter exceeding 5 mm on MRI or the presence of morphologic predictors of LPN metastasis, such as heterogeneous signal intensity or a spiculated or indistinct border of the nodal capsule [22]. These diagnostic criteria for LPN evaluation remained consistent throughout the study.

The patients received a conventional preoperative fluoropyrimidine-based long-course nCRT regimen [23]. The preoperative radiotherapy dose was 45 Gy in 25 fractions to the pelvis over 5.5 weeks; the boost dose was 5.4 Gy in 3 fractions to the primary tumor. Capecitabine or fluorouracil and leucovorin combination therapy was used as concurrent chemotherapy. The clinical response was evaluated with pelvic MRI repeated approximately 5–7 weeks after the completion of nCRT.

Radical surgery, including sphincter-preserving surgery or abdominoperineal resection, was performed 6–8 weeks after the completion of nCRT. All surgeries were performed by experienced certified colorectal surgeons. The decision to perform LPND with radical surgery was based on the response of LPNs to nCRT. If LPN metastasis was no longer suspected after completing nCRT, TME alone was performed; otherwise, TME and LPND were performed together.

All patients in the responsive group were reassessed by a multidisciplinary team (MDT), which included colorectal surgeons, medical oncologists, radiation oncologists, and specialized gastrointestinal radiologists. The decision to omit or perform LPND was based on 2 explicit MRI criteria: (1) post-nCRT LPN SA diameter ≤5 mm; and (2) absence of morphologic predictors of malignancy, specifically heterogeneous signal intensity, irregular margins, or indistinct borders of the lymph node capsule. If morphologic predictors persisted despite adequate size reduction, TME with LPND was performed to ensure oncologic completeness.

Outcomes

The primary outcome was the LR rate of mid/low rectal cancer in patients who underwent nCRT followed by selective LPND. Secondary outcomes included various surgicopathological outcomes, such as operative time, intraoperative blood loss, and postoperative complications. Additionally, pathological outcomes including the number of retrieved lymph nodes and the presence of residual tumor in resected lymph nodes were assessed. Oncologic outcomes including 5-year overall survival (OS), disease-free survival (DFS), and systemic metastasis rates were also evaluated. Subgroup analysis was conducted to compare these outcomes among different patient groups based on their LPN status post-nCRT.

Statistical analyses

Continuous variables are expressed as means ± standard deviations or medians and interquartile ranges, depending on the normality of distribution. Categorical variables are expressed as frequencies (percentages). Continuous variables were compared using the Student t-test or the Mann-Whitney U-test, whereas categorical variables were compared using the chi-square or Fisher exact tests. The survival rates in the responsive and persistent groups were estimated using the Kaplan-Meier method and visualized with survival curves. The survival rates between the 2 groups were compared using the log-rank test. A P-value <0.05 was considered statistically significant. All data were analyzed using IBM SPSS Statistics for Windows, ver. 27.0 (IBM Corp.) and R (ver. 3.3.3, The R Foundation).

RESULTS

Patient characteristics

In our study population, 128 patients demonstrated clinically suspicious LPN metastasis before receiving nCRT. Of these, 5 patients who underwent emergency surgery and one patient who underwent local excision were excluded, resulting in 122 patients being included in the final analysis. Among them, 82 (67.2%) and 40 (32.8%) were classified into the responsive and persistent groups, respectively. The distribution of surgical procedures among patients in responsive and persistent groups is presented in Fig. 1. The median follow-up period was 55.4 months (interquartile range, 30.0–72.0 months).

The groups did not differ in preoperative baseline demographics (Table 1). Likewise, the preoperative CEA levels did not differ, although the postoperative CEA levels were higher in the responsive than in the persistent group (1.4 ± 1.2 ng/mL *vs.* 1.0 ± 0.7 ng/mL, P = 0.020). The responsive group had a lower ycN positive rate than the persistent group (41.5% *vs.* 97.5%, P < 0.001). Although the change in LPN size between pre- and post-nCRT was greater in the persistent group (5.2 ± 2.8 mm *vs.* 2.0 ± 2.3 mm, P < 0.001), the sizes of pre-nCRT and post-nCRT LPNs were smaller in the responsive group (7.4 ± 1.9

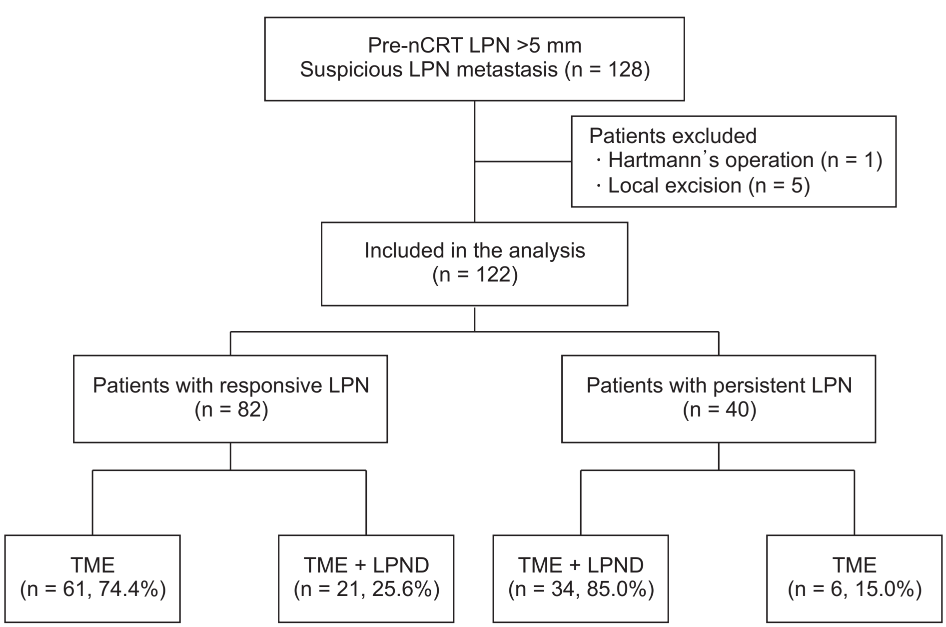

Fig. 1. Flowchart of the study population. nCRT, neoadjuvant chemoradiotherapy; LPN, lateral pelvic node; TME, total mesorectal excision; LPND, lateral pelvic lymph node dissection.

Table 1. Baseline characteristics of included patients

Characteristic	Responsive group	Persistent group	P-value
No. of patients	82	40	
Sex			0.385
Male	53 (64.6)	29 (72.5)	
Female	29 (35.4)	11 (27.5)	
Age (yr)			0.167
<50	19 (23.2)	14 (35.0)	
≥50	63 (76.8)	26 (65.0)	
Body mass index (kg/m^2)	24.5 ± 3.1	24.1 ± 3.7	0.482
ASA PS class			0.836
I	18 (22.0)	8 (20.0)	
II	62 (75.6)	32 (80.0)	
III	2 (1.6)	0 (0)	
Tumor location from the AV (cm)			0.494
>5	21 (25.6)	8 (20.0)	
≤5	61 (74.4)	32 (80.0)	
Preoperative chemotherapy			0.346
Capecitabine	73 (89.0)	38 (95.0)	
5-FU and leucovorin	8 (9.8)	1 (2.5)	
FOLFOX/XELOX	1 (1.2)	1 (2.5)	
Adjuvant chemotherapy			0.069
No	8 (9.8)	1 (2.5)	
5-FU or capecitabine	33 (40.2)	10 (25.0)	
FOLFOX/XELOX/FOLFIRI	38 (46.3)	25 (62.5)	
Unknown	3 (2.5)	4 (10.0)	
cT stage			0.626
0 or I	1 (1.2)	0 (0)	
2	2 (2.4)	0 (0)	
3	57 (69.5)	32 (80.0)	
4	22 (26.8)	8 (20.0)	
CEA concentration (ng/mL)			
Preoperative	4.7 ± 13.4	4.0 ± 10.9	0.784
Postoperative	1.4 ± 1.2	1.0 ± 0.7	0.020
LPN size (mm)			
Pre-nCRT	7.4 ± 1.9	10.5 ± 4.7	<0.001
Post-nCRT	2.2 ± 2.2	8.4 ± 4.3	<0.001
Change, pre–post	5.2 ± 2.8	2.0 ± 2.3	<0.001
ycT stage			0.715
0 or 1	3 (3.7)	2 (5.0)	
2	13 (15.9)	8 (20.0)	
3	47 (57.3)	24 (60.0)	
4	19 (23.3)	6 (15.0)	
ycN stage			<0.001
0	48 (58.5)	1 (2.5)	
Positive	34 (41.5)	39 (97.5)	
LPN location			0.241
Unilateral	56 (68.3)	23 (57.5)	
Bilateral	26 (31.7)	17 (42.5)	
LPN region			0.460
Internal iliac	54 (65.9)	29 (72.5)	
Others	28 (34.1)	11 (27.5)	

Values are presented as number only, number (%), or mean ± standard deviation.
ASA PS, American Society of Anesthesiologists physical status; AV, anal verge; 5-FU, 5-fluorouracil; FOLFOX, oxaliplatin/5-FU/leucovorin; XELOX, capecitabine/oxaliplatin; FOLFIRI, irinotecan/5-FU/leucovorin; LPN, lateral pelvic node; nCRT, neoadjuvant chemoradiotherapy.

Table 2. Surgicopathological and oncologic outcomes in patients

Variable	Responsive group (n = 82)	Persistent group (n = 40)	P-value
Operation type			0.266
Laparoscopic	72 (87.8)	32 (80.0)	
Open	10 (12.2)	8 (20.0)	
Operation			0.749
Sphincter-preserving operation	70 (85.4)	35 (87.5)	
Abdominoperineal resection	12 (14.6)	5 (12.5)	
Operative time (min)	286.3 ± 111.5	315.0 ± 85.4	0.154
Estimated blood loss (mL)	236.7 ± 470.3	192.5 ± 319.3	0.593
Length of hospital stay (day)	10.4 ± 6.9	10.7 ± 5.7	0.833
Postoperative 30 days complications			0.693
Yes	68 (82.9)	32 (80.0)	
No	14 (17.1)	8 (20.0)	
Pathologic results			
Tumor size (cm)	2.5 ± 1.7	3.0 ± 2.0	0.186
Distal resection margin (cm)	2.3 ± 2.4	2.7 ± 4.3	0.498
Circumferential resection margin (mm)			0.759
Negative, >1	62 (88.6)	31 (86.1)	
Positive, ≤1	8 (11.4)	5 (13.9)	
Lymphatic invasion			>0.999
Yes	9 (11.8)	4 (10.3)	
No	67 (88.2)	35 (89.7)	
Venous invasion			0.021
Yes	4 (5.3)	8 (20.5)	
No	72 (94.7)	31 (79.5)	
Perineural invasion			0.526
Yes	21 (27.6)	13 (33.3)	
No	55 (72.4)	26 (66.7)	
Histologic grade			0.715
Well	5 (6.1)	3 (7.7)	
Moderate	69 (84.1)	34 (87.2)	
Poor/mucinous/signet ring cell	8 (9.8)	2 (5.1)	
Harvested lymph nodes	33.8 ± 11.7	32.3 ± 11.8	0.491
ypT stage			0.788
T0–1	18 (22.0)	7 (17.5)	
T2	18 (22.0)	9 (22.5)	
T3	43 (52.4)	21 (52.5)	
T4	3 (3.7)	3 (7.5)	
ypN stage			<0.001
N0	57 (69.5)	14 (35.0)	
N1–2	25 (30.5)	26 (65.0)	
Harvested LPNs	7.1 ± 4.2	5.1 ± 3.9	0.069[a]
Pathological LPN			0.046[a]
No metastasis	17 (81.0)	18 (52.9)	
Metastasis	4 (19.0)	16 (47.1)	
Tumor regression grade			>0.999
Dworak grade 0–2	54 (65.9)	27 (67.5)	
Dworak grade 3–4	28 (34.1)	13 (32.5)	
Median FU (mo)	47.6 ± 27.2	44.2 ± 28.2	0.519
Locoregional recurrence			0.003
Yes	0 (0)	4 (10.0)	
No	82 (100)	36 (90.0)	
Systemic metastasis			0.812
Yes	11 (13.4)	6 (15.0)	
No	71 (86.6)	34 (85.0)	

Values are presented as number (%) or mean ± standard deviation.
Missing data: lymphatic invasion, venous invasion, perineural invasion; responsive group (n = 6), persistent group (n = 1).
FU, follow-up; LPN, lateral pelvic node.
[a]The denominator is the comparison of patients who underwent lateral pelvic node dissection by the Pearson chi-square test and Student t-test.

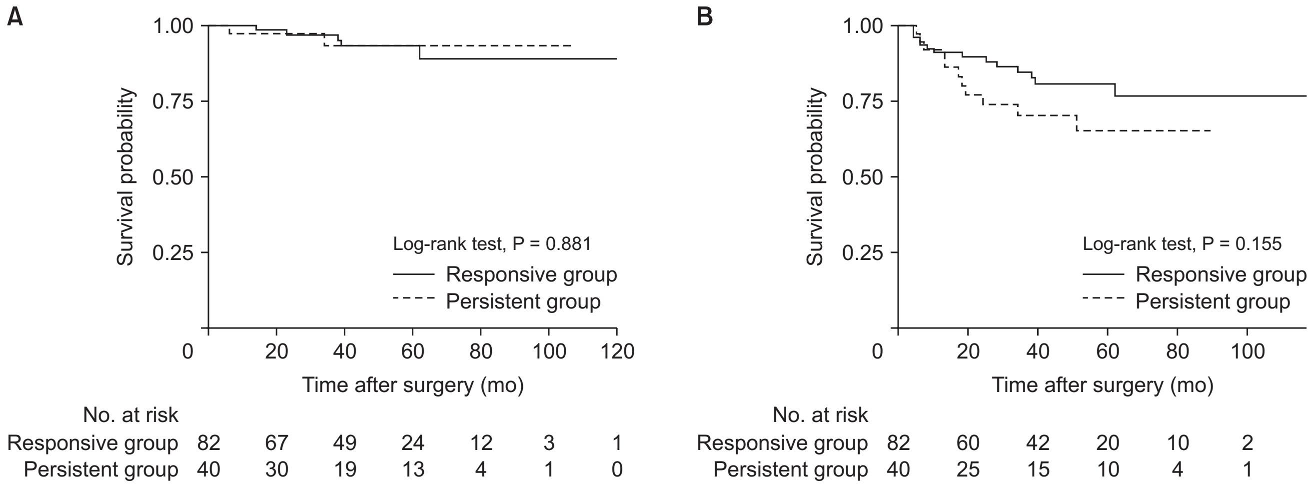

Fig. 2. Kaplan-Meier analysis of patient survival. (A) Overall survival and (B) disease-free survival comparing patients according to patient groups. Responsive group, post-nCRT LPND ≤5 mm. Persistent group, post-nCRT LPND >5 mm. LPND, lateral pelvic lymph node; nCRT, neoadjuvant chemoradiotherapy.

mm *vs.* 10.5 ± 4.7 mm, P < 0.001; 2.2 ± 2.2 mm *vs.* 8.4 ± 4.3 mm, P < 0.001).

Surgicopathological and oncologic outcomes

Most surgical and pathological outcomes did not differ significantly between the responsive and persistent groups (Table 2), although the rate of venous invasion was higher in the persistent group (20.5% *vs.* 5.3%, P = 0.021). The total number of lymph nodes harvested did not differ significantly between groups, although the rate of metastatic lymph nodes was higher in the persistent group (65.0% *vs.* 30.5%, P < 0.001). The pathological LPN status was evaluated only in patients who underwent both TME and LPND. The total number of harvested LPNs did not differ between groups, although the rate of metastatic LPNs was higher in the persistent group than in the responsive group (19.0% *vs.* 47.1%, P = 0.046). Of 55 patients who underwent LPND, 20 (36.4%) showed pathological LPN metastasis, and the LPN metastasis rate was higher in the persistent than in the responsive group (47.1% *vs.* 19.0%, P = 0.046). The median follow-up period did not differ between the 2 groups. LR was observed only in the persistent group (10.0%, P = 0.003), and systemic metastasis rates were similar between groups.

Five-year OS and DFS rates did not differ between responsive and persistent groups (93.4% *vs.* 93.5%, P = 0.881; 81.0% *vs.* 65.3%, P = 0.155, respectively) (Fig. 2). LR was reported in 4 patients (3.3%), all of whom were in the persistent group and had undergone LPND. Systemic metastasis was reported in 17 patients (13.9%), with no significant difference in the rate of systemic metastasis between the responsive and persistent groups (13.4% *vs.* 15.0%, P = 0.812). In the 4 patients with LR, postoperative pathology revealed no viable tumors in the resected LPNs. The LR site was the lateral pelvic wall in all 4 patients, with one patient also showing LR at the anastomotic site.

Subgroup analysis: responsive group

Baseline characteristics were similar between the TME alone and TME + LPND subgroups (Table 3). The median follow-up period was comparable between the TME alone and TME + LPND subgroups (46.8 ± 27.2 months *vs.* 50.1 ± 27.9 months). The pre-nCRT LPN size was significantly smaller in the TME alone subgroup (7.1 ± 1.6 mm *vs.* 8.3 ± 2.5 mm, P = 0.043), and the post-nCRT LPN size was also significantly smaller in this subgroup (1.7 ± 2.1 mm *vs.* 3.9 ± 1.8 mm, P < 0.001). The ycN positive rate was significantly higher in the TME + LPND subgroup than in the TME alone subgroup (71.4% *vs.* 31.1%, P = 0.001) (Table 4). LR was not observed in either subgroup, and systemic metastasis rates were equivalent in the TME alone and TME + LPND subgroups.

DISCUSSION

This study evaluated the surgicopathological and oncologic outcomes of LPND in patients with mid/low rectal cancer, based on the LPN response to nCRT. The findings suggest that selective LPND, guided by post-nCRT LPN size and morphologic predictors of metastasis, could be a feasible strategy.

Currently, several strategies have been proposed for LPND in rectal cancer with suspected metastatic LPNs. The first is routine bilateral LPND if LPN enlargement is present on pretreatment MRI before nCRT, with efficacy reported mainly in Japanese studies [24,25]. However, due to high comorbidity and adverse effects including urinary and sexual dysfunction, routine LPND is considered overtreatment. Therefore, 2 criteria for selective LPND were proposed: suspicion of metastatic LPN

Table 3. Baseline characteristics of TME alone and TME + LPND subgroups within the responsive group

Characteristic	TME alone	TME + LPND	P-value
No. of patients	61	21	
Sex			0.173
Male	42 (68.9)	11 (52.4)	
Female	19 (31.1)	10 (47.6)	
Age (yr)			>0.999
<50	14 (23.0)	5 (23.8)	
≥50	47 (77.0)	16 (76.2)	
Body mass index (kg/m^2)	24.6 ± 3.4	24.3 ± 2.2	0.585
ASA PS class			0.749
I	12 (19.7)	6 (28.6)	
II	47 (77.0)	15 (71.4)	
III	2 (3.3)	0 (0)	
Tumor location from the AV (cm)			>0.999
>5	16 (26.2)	5 (23.8)	
≤5	45 (73.8)	16 (76.2)	
Preoperative chemotherapy			0.757
Capecitabine	53 (86.9)	20 (95.2)	
5-FU and leucovorin	7 (11.5)	1 (4.8)	
FOLFOX/XELOX	1 (1.6)	0 (0)	
cT stage			0.910
0 or I	1 (1.6)	0 (0)	
2	2 (3.3)	0 (0)	
3	41 (67.2)	16 (76.2)	
4	17 (27.9)	5 (23.8)	
CEA concentration (ng/mL)			
Preoperative	3.8 ± 7.6	7.4 ± 23.7	0.506
Postoperative	1.5 ± 1.2	1.3 ± 1.2	0.452
LPN size (mm)			
Pre-nCRT	7.1 ± 1.6	8.3 ± 2.5	0.043
Post-nCRT	1.7 ± 2.1	3.9 ± 1.8	<0.001
Change, pre–post	5.4 ± 2.6	4.4 ± 3.4	0.180
ycT stage			0.849
0 or 1	3 (4.9)	(0.0)	
2	10 (16.4)	3 (14.3)	
3	35 (57.4)	12 (57.1)	
4	13 (21.3)	6 (28.6)	
ycN stage			0.001
0	42 (68.9)	6 (28.6)	
Positive	19 (31.1)	15 (71.4)	
LPN location			0.466
Unilateral	43 (70.5)	13 (61.9)	
Bilateral	18 (29.5)	8 (38.1)	
LPN region			0.329
Internal iliac	42 (68.9)	12 (57.1)	
Other	19 (31.1)	9 (42.9)	

Values are presented as number only, number (%), or mean ± standard deviation.
TME, total mesorectal excision; LPND, lateral pelvic node dissection; ASA PS, American Society of Anesthesiologists physical status; AV, anal verge; 5-FU, 5-fluorouracil; FOLFOX, oxaliplatin/5-FU/leucovorin; XELOX, capecitabine/oxaliplatin; LPN, lateral pelvic node; nCRT, neoadjuvant chemoradiotherapy.

on pretreatment images and poor nCRT response. Many studies have reported on the outcomes of LPND based on LPN size on pretreatment MRI. Bae et al. [26] proposed optimal indications for LPND as an initial LPN size >8 mm or >6 mm for tumors located >5 cm or ≤5 cm from the anal verge, respectively. Other studies have also reported a benefit to local control with LPND in the presence of enlarged LPNs prior to nCRT, with cutoff sizes varying from 5 to 10 mm [27-29].

Table 4. Surgicopathological and oncologic outcomes of TME alone and TME + LPND subgroups within the responsive group

Variable	TME alone (n = 61)	TME + LPND (n = 21)	P-value
Operation type			0.269
Laparoscopic	55 (90.2)	17 (81.0)	
Open	6 (9.8)	4 (19.0)	
Operation			0.280
Sphincter-preserving operation	54 (88.5)	16 (76.2)	
Abdominoperineal resection	7 (11.5)	5 (23.8)	
Operative time (min)	261.3 ± 79.3	358.8 ± 154.9	<0.001
Estimated blood loss (mL)	203.9 ± 402.0	331.9 ± 631.2	0.285
Length of hospital stay (day)	10.1 ± 6.9	11.2 ± 7.0	0.527
Postoperative 30 days complications			0.503
Yes	51 (83.6)	16 (76.2)	
No	10 (16.4)	5 (23.8)	
Pathologic results			
Tumor size (cm)	2.6 ± 1.7	2.5 ± 1.6	0.853
Distal resection margin (cm)	2.0 ± 1.6	3.2 ± 3.7	0.156
Circumferential resection margin (mm)			0.433
Negative, >1	44 (86.3)	18 (94.7)	
Positive, ≤1	7 (13.7)	1 (5.3)	
Lymphatic invasion			>0.999
Yes	7 (12.3)	2 (10.5)	
No	50 (87.7)	17 (89.5)	
Venous invasion			0.567
Yes	4 (7.0)	0 (0)	
No	53 (93.0)	19 (100)	
Perineural invasion			0.183
Yes	18 (31.6)	3 (15.8)	
No	39 (68.4)	16 (84.2)	
Histologic grade			0.767
Well	4 (6.6)	1 (4.8)	
Moderate	52 (85.2)	17 (81.0)	
Poor/mucinous/signet ring cell	5 (8.2)	3 (14.3)	
Harvested lymph nodes	31.1 ± 11.0	41.6 ± 10.6	<0.001
ypT stage			0.818
T0–1	14 (23.0)	4 (19.0)	
T2	12 (19.7)	6 (28.6)	
T3	32 (52.5)	11 (52.4)	
T4	3 (4.9)	0 (0)	
ypN stage			0.380
N0	44 (72.1)	13 (61.9)	
N1–2	17 (27.9)	8 (38.1)	
Pathological LPN			
No metastasis		17 (81.0)	
Metastasis		4 (19.0)	
Harvested lateral lymph nodes		7.1 ± 4.2	
Tumor regression grade			0.322
Dworak grade 0–2	38 (62.3)	16 (76.2)	
Dworak grade 3–4	23 (37.7)	5 (23.8)	
Median FU (mo)	46.8 ± 27.2	50.1 ± 27.9	
Locoregional recurrence			
Yes	0 (0)	0 (0)	
No	61 (100)	21 (100)	
Systemic metastasis			>0.999
Yes	8 (13.1)	3 (14.3)	
No	53 (86.9)	18 (85.7)	

Values are presented as number (%) or mean ± standard deviation.
Missing data: lymphatic invasion, venous invasion, perineural invasion; responsive group (n = 4), persistent group (n = 2).
TME, total mesorectal excision; LPND, lateral pelvic node dissection; LPN, lateral pelvic node; FU, follow-up.

However, relatively few reports have examined more selective LPND based on nCRT responses. Kim et al. [30] reported that LPN recurrence-free survival was significantly lower in the persistent group (LPN ≥5 mm pre- and post-nCRT), whereas relapse-free survival and OS were comparable between the responsive and non-suspicious LPN groups (LPN <5 mm pre- and post-nCRT), suggesting no benefit of LPND for nCRT-responsive LPNs (LPN ≥5 mm pre-nCRT but <5 mm post-nCRT). Malakorn et al. [31] also reported that no pathologically positive LPNs were found if the size of LPNs after nCRT was <5 mm, suggesting that LPND should be performed only if post-nCRT LPN size is >5 mm. However, their study included only 66 patients and could not clarify all conditions under which LPND can be omitted. A large multicenter retrospective study in China found that a post-nCRT LPN size >7 mm and poor tumor differentiation were independent predictors of LPN metastasis, suggesting that both factors should be considered when selecting candidates for LPND [32].

Our study did not omit LPND based solely on post-nCRT LPN size. Instead, we adopted a tailored strategy, omitting LPND in cases where the post-nCRT LPN size was reduced to ≤5 mm and no morphologic predictors of LPN metastasis were present. Conversely, LPND was performed if morphologic predictors were identified, even when LPN size was reduced. This approach resulted in no LR, demonstrating the efficacy of this treatment strategy. Within the responsive group, patients who underwent TME alone exhibited near-complete regression and higher ycN-negativity rates compared to those who underwent TME with LPND, further supporting the selective approach. Although pathological LPN metastases were confirmed in approximately 19% of responsive patients undergoing selective LPND, local recurrence was not observed during the follow-up period (median, 55 months). Potential explanations for this finding include the effective removal of metastatic nodes by selective LPND, adequate control of microscopic residual malignancy by nCRT, and rigorous postoperative surveillance contributing to the prevention of clinically detectable recurrence. Similar phenomena have been documented previously, supporting the potential effectiveness of selective LPND guided by size reduction and morphological criteria. Further prospective studies are warranted to validate these findings.

Our results are consistent with the findings of prior studies [30,31], highlighting that considering both LPN size reduction and morphological predictors effectively prevents LR while minimizing unnecessary surgeries. The importance of pre-nCRT lymph node size should also be considered. In this study, pre-nCRT lymph node size was significantly larger in the persistent group than in the responsive group, suggesting a potentially higher initial metastatic burden. Previous studies have also highlighted pretreatment lymph node size as an important predictor of malignancy; however, lymph nodes exhibiting substantial size reduction after nCRT frequently present nonviable fibrotic or reactive changes rather than residual tumor cells. Thus, selective omission of LPND for lymph nodes reduced to ≤5 mm with favorable morphology may safely reduce unnecessary surgical morbidity without negatively impacting oncologic outcomes. Further prospective validation studies are needed to confirm these results.

Several studies have focused on predicting tumor-harboring LPNs using morphological criteria. Brown et al. reported high accuracy for morphologic predictors in patients with rectal cancer, with irregular margins or mixed signal intensity on MRI showing high sensitivity and specificity [33]. The MERCURY group [22] reported that patients with suspicious malignant pelvic side wall lymph nodes had poorer 5-year DFS compared to those without (31.0% *vs.* 76.3%, $P < 0.001$). In our study, preoperative MDT discussions considered these morphological predictors to decide on LPND. The comparable oncologic outcomes in the responsive group suggest that both LPN size and morphologic features should be used to guide LPND decisions. Our findings reinforce the importance of evaluating both size and morphological changes post-nCRT for informed decisions regarding LPND. However, as previously acknowledged, the accurate differentiation of residual malignancy from radiation-induced benign changes, such as fibrosis or edema, remains challenging, particularly for small-sized lymph nodes (≤5 mm) post-nCRT. Recognizing these inherent limitations, our study relied on comprehensive MDT evaluations integrating radiologic findings and clinical contexts to minimize potential misclassification. Further improvements in differentiating malignant from benign lymph nodes may require the integration of advanced MRI techniques, such as diffusion-weighted imaging, or artificial intelligence-driven radiomics analyses.

Few studies have compared the rate of pathological LPN metastasis according to nCRT response in patients undergoing TME with LPND and its association with oncologic outcomes. A previous study reported a 0% pathological LPN rate in the responsive group undergoing LPND [21]. In Kim et al.'s study [29], the responsive group had a lower pathological LPN rate (16.7% *vs.* 65.2%, $P < 0.001$) and a lower 3-year LR rate (0.0% *vs.* 18.8%, $P = 0.001$) than the unresponsive group. Similarly, our study showed a lower rate of pathological metastatic LPNs in the responsive group (19.0% *vs.* 47.1%, $P = 0.046$) and a lower LR rate (0.0% *vs.* 10.0%, $P = 0.003$), supporting the selective use of LPND based on nCRT response. Although Kim et al. [29] suggested that LPND should be performed in all patients, regardless of their nCRT response, our findings indicate that selectively omitting LPND in patients with significant LPN size reduction and no morphologic predictors can achieve favorable oncologic outcomes.

However, in the persistent group, LPND was omitted in patients where extensive surgery could not be performed due to comorbidities or when benign tumors were highly probable based on imaging tests such as MRI. Among the 6 patients without LPND, no LR occurred, and one patient developed systemic metastasis, but the sample size was insufficient for statistical significance. These results suggest that in certain cases where surgery is not viable, careful surveillance and imaging can help manage the disease without immediate LPND.

This study has several limitations. The lack of protocol consistency remains a significant limitation, as the protocol for performing LPND was not uniformly applied according to predefined criteria. Treatment decisions depended on each patient's individual characteristics and comorbidities, the size of the LPN, MRI findings, and other test results. These decisions were made after MDT discussions, which overcame some of the limitations to some extent, but the retrospective cohort design may have introduced selection bias by only including patients who completed nCRT and had an MRI. In addition, the relatively small sample size from a single institution limits the ability to draw definitive conclusions. The study also relies on historical data from our institution, where LPND indications were based on previous research outcomes, which may not be generalizable.

Additionally, the absence of a control group limits the ability to definitively assess the impact of LPND on survival and recurrence rates. Specifically, this study adopted a strategy of omitting LPND in cases of post-nCRT LPN size reduction but performing LPND when morphologic predictors of metastasis were present. This approach makes it difficult to determine whether LR absence is due to LPN size reduction, morphologic factors, or both. A control group to compare these variables independently is lacking, which is a significant limitation. Another limitation is the long data collection period from 2012 to 2022, during which advancements in nCRT protocols occurred. To address these limitations, future research should aim to standardize the LPND protocol, incorporate multicenter data to enhance generalizability, and include control groups for a more robust comparison. Moreover, prospective studies with longer follow-up periods and larger sample sizes are needed to fully evaluate the long-term outcomes and validate the findings of this study. Further subgroup analyses should investigate additional factors influencing clinical outcomes beyond LPN size. Furthermore, given the retrospective design of this study, the precise quantitative documentation of morphological predictors for individual patients was not systematically performed, limiting detailed subgroup analyses. Some patients who underwent TME alone might indeed have had morphological predictors, but LPND was omitted due to advanced age, significant comorbidities, or patient refusal. Prospective studies systematically documenting morphological predictors are necessary to validate and refine this selective approach.

In conclusion, selective LPND may serve as a feasible treatment option for managing mid/low rectal cancer with enlarged LPNs, particularly when guided by a good response to nCRT (post-nCRT LPN size ≤5 mm) and the absence of morphologic predictors of metastasis. TME alone demonstrated local control and systemic metastasis rates comparable to those achieved with TME + LPND in the responsive group. This selective approach appears to offer the potential for optimizing treatment strategies while potentially reducing surgical interventions, especially in cases showing a significant reduction in LPN size and lower ycN positivity rates following nCRT.

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Conflict of Interest

Duck-Woo Kim, serving as the Editor-in-Chief of *Annals of Surgical Treatment and Research*, is the corresponding author of this article. To ensure an unbiased review process, Professor Kim did not participate in the editorial evaluation of this manuscript, and an independent handling editor was appointed. No other potential conflicts of interest relevant to this article were reported.

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