https://doi.org/10.33878/2073-7556-2025-24-4-46-52

Lateral pelvic lymph node dissection for rectal cancer after neoadjuvant chemoradiotherapy. Results of a prospective study

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ABSTRACT *AIM: to evaluate the early results of selective lateral pelvic lymph node dissection (LPLD) in patients with middle and low rectal cancer after neoadjuvant CRT with suspected lateral lymph nodes (LLN) involvement based on MRI data.*
PATIENTS AND METHODS: a prospective single-arm single-center study included 70 patients with a verified diagnosis of rectal cancer (mrT1–4N1–2cM0–1) who underwent total mesorectal excision (TME) with LTLD after neoadjuvant chemotherapy between January 2023 and May 2025. Intraoperatively, all patients underwent fluorescent navigation with indocyanine green and LLN ultrasound. The primary endpoint was the presence of metastases in the LLN based on histology. Secondary endpoints included: sensitivity and specificity of MRI in detecting LLN metastases, postoperative morbidity, local recurrence rate, operation time, blood loss, hospital stay, and the relationship between LLN size and the presence of metastases.
RESULTS: in 23/70 (33%) patients, metastatic involvement of the LLN was confirmed. The sensitivity and specificity of MRI were 91% (95% CI: 72.0%–98.9%) and 38% (95% CI: 24.5%–53.6%). A comparison of the median short axis in patients with metastatic LLN involvement (9.2 (7.8; 11.3) mm) and in patients without metastasis (5.4 (4.2; 6.5) mm) revealed a significant difference ($p < 0.001$). The operation time was 210 (170; 265) minutes, and total blood loss was 60 (30; 120) ml. Clavien–Dindo grade I-II complications detected in 16/70 (23%) patients. No cases required re-operation. The hospital stay was 12 (10; 16) days. Local recurrences revealed in 3/70 (4%) patients with follow-up of 14 (8; 20) months.
CONCLUSION: selective LPLD after neoadjuvant HLT is a potentially effective method for reducing the risk of local recurrence in patients with suspected LLN involvement in rectal cancer. However, randomised controlled trials with a long follow-up period are needed to definitively assess its contribution to improving late outcomes.

KEYWORDS: *rectal cancer, lateral pelvic lymph node dissection, lateral pelvic lymph nodes, local recurrence of rectal cancer, neoadjuvant chemoradiotherapy*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

FOR CITATION: Tishkevich I.S., Alekseev M.V., Khomyakov E.A., Zakharkina E.N., Rybakov E.G. Lateral pelvic lymph node dissection for rectal cancer after neoadjuvant chemoradiotherapy. Results of a prospective study. *Koloproktologia*. 2025;24(4):46–52. (in Russ.). https://doi.org/10.33878/2073-7556-2025-24-4-46-52

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Received — 01.08.2025 *Revised — 27.08.2025* *Accepted for publication — 10.11.2025*

INTRODUCTION

The incidence of lateral pelvic lymph nodes (LPLN) involvement in rectal cancer increases in inverse proportion to the height of the tumor from the anal margin and, according to some authors, when the tumor is localized in the low rectum, reaches 29.6% [1]. LPLN metastases are the most common cause of locoregional recurrences, which occur in 25.6% vs 6.8% in patients without them ($p < 0.0001$). This fact is naturally reflected in the overall survival rates, which deteriorates in the group of patients with affected lymph nodes (45.8% versus 71.2% in the group of patients in whom these lymph nodes are not affected, $p < 0.0001$) [2].

Routine lateral pelvic lymphnodes dissection (LPLD) is not standard approach for colorectal cancer in Russia and Western countries. However, some studies have reported improved local control when using LPLD after neoadjuvant CRT. So, in a study by Akiyoshi et al., with a median follow-up of 47.5 (3.5–105.4) months, local recurrence occurred in 3 of 89 (3.4%) patients in the group who underwent total mesorectumectomy (TME) after neoadjuvant chemoradiotherapy (CRT) and none (0/38) when LPLD was added [3]. In eastern countries, in particular, in South Korea and Japan, lateral pelvic lymph dissection is the standard and is performed routinely, regardless of the presence or absence of metastases in the lymph nodes. However, this procedure is associated with an increased risk of complications such as intraoperative bleeding, urinary disorders, and sexual dysfunction [4,5,6].

Thus, there is no unified approach to the treatment of patients with rectal cancer affected by LPLN.

In the presented study, we studied the early results of LPLD in patients with cancer of the middle and low rectum who underwent neoadjuvant CRT.

PATIENTS AND METHODS

In the period from January 2023 to May 2025, 70 patients underwent radical surgery for cancer of the middle and low rectum (TME and LPLD after neoadjuvant CRT). *The criteria for inclusion* in this prospective single-group study were patients with C20, mrT1-4N1-2cM0-1 and tumor site in the middle or low rectum with suspected LPLN lesion according to pelvic MRI before neoadjuvant CRT or RT.

The criteria for non-inclusion were: absence of suspicious LPLN according to pelvic MRI; unresectable locally advanced or symptomatic metastases; somatic or psychiatric contraindications to surgery and/or general anesthesia; previous pelvic surgery that can distort the anatomy of regional lymph drainage; pregnancy and lactation period.

The exclusion criteria: the patient's refusal to continue participating in the study at any stage; identification of another malignant disease unrelated to rectal cancer; retrospectively established non-compliance with the inclusion criteria; inability to perform histology of the removed LPLN due to technical reasons.

LPLNs were considered suspicious in the presence of one or more of the following signs: diameter of the lymph node along the short axis ⩾ 7 mm; uneven or fuzzy contours; heterogeneous structure in T2-weighted images; lack of central hypointensity; increased signal in diffusion-weighted images (DWI) combined with a reduced diffusion coefficient (ADC), as well as the presence of heterogeneous or intensive accumulation of contrast agent with dynamic contrast enhancement. The stage of the disease was assessed based on colonoscopy, computed tomography of the chest and abdominal organs, and magnetic resonance imaging of the pelvic organs. Each patient was discussed at a multidisciplinary consultation, which included an oncologist, a chemotherapist, a radiotherapist, and a radiologist to determine treatment approach.

All operations were elective epidural anesthesia + intravenous sedation + ALV. All patients underwent intraoperative ultrasound of the LPLN intraoperatively in order to identify them. All patients underwent fluorescent navigation with indocyanine green (ICG) as well to control lymph nodes lesion [8]. The ICG (25 mg) was dissolved in 10 ml of sterile water for injection, obtaining a solution with a concentration of 2.5 mg/ml. Paratumoral injection of ICG was performed transanally 1–2 hours before LPLD into the submucosal layer of the rectal wall at 3–4 points near the tumor. The injection volume was 0.5 ml at each point, which combined to provide 1.5–2 ml of solution (3.75–5 mg ICG). During LPLD, lymph nodes were visualized using a laparoscopic system equipped with an infrared camera capable for detecting fluorescence in the near infrared range. The severity of postoperative morbidity was assessed using Clavien-Dindo's scale [7]. The characteristics of the patients and the treatment performed are presented in Table 1.

Table 1. *Baseline characteristics of patients and treatment*

Indicators	Total patients N = 70
Age, years, median (Q1; Q3)	57 (41; 65)
Gender	
Male	45 (64%)
Female	25 (36%)
Localization of the primary tumor	
The middle rectum	27 (38%)
Low rectum	43 (62%)
TNM	
ypT1-2N0	20 (29%)
ypT1-2N+	5 (7%)
ypT3-4N0	27 (39%)
ypT3-4N+	18 (26%)
The tumor differentiation grade	
G1	3 (4%)
G2	48 (69%)
G3	19 (27%)
Chemoradio therapy	
Prolonged course (50-54 Gy)	54 (77%)
Short course (25 Gy)	16 (23%)
Consolidating chemo therapy	
Egimen XELOX	29 (41%)
RegimenFOLFOX-6	25 (36%)
Not conducted	16 (24%)
Surgery type	
Low anterior resection	32 (46%)
Intrashincter resection	10 (14%)
Abdominal-perineal excision	23 (33%)
Hartmann's procedure	4 (6%)
Proctocolectomy	1 (1%)

The primary endpoint was the incidence of metastatic lesion of removed LPLN by pathomorphology. The secondary endpoints were: — sensitivity and specificity of MRI in the diagnosis of metastatic lesion of LPLN; — the incidence of postoperative morbidity by Clavien-Dindo's scale; — the locoregional recurrences rate; — the operative time and intraoperative blood loss; — postoperative hospital stay; — LPLN size depending on the presence or absence of metastases.

Statistical Analysis

All the data analyzed in the study were entered into an Excel spreadsheet (Microsoft Office 2016). The statistical analysis was performed in the Statistica program v.13.3 (TIBCO, USA). Qualitative features were described in the form of absolute and relative rates (*n* (%) or n/N (%)); quantitative in the form of median (Me), lower and upper quartiles (Q1; Q3), minimum and maximum values (Min-Max). The groups were compared by quantitative parameter using Mann-Whitney's U-test. To assess the diagnostic significance of MRI, sensitivity and specificity were calculated with a 95% coincidence interval (CI) calculated using Clopper-Pearson's method. The differences were considered statistically significant at $p < 0.05$.

RESULTS

All 70 patients included in the study underwent total mesorectumectomy in combination with lateral pelvic lymphodissection after neoadjuvant chemoradiotherapy. The surgery was performed by laparoscopic access in 42/70 (60%) patients. In 25/70 (36%) of the cases, bilateral LPLD was performed, in 25/70 (36%) — left-sided, and in 20/70 (28%) — right-sided LPLD. One patient developed cancer against the background of a classic form of familial adenomatosis of the large intestine with a confirmed mutation in the *APC* gene. He underwent a proctocolectomy with J-pouch and pouch-anal anastomosis and preventive ileostomy. Before the surgery, 50/70 (71%) patients showed metastatic lesion of the LPLN according to the MRI. After LPLD, according to the pathomorphological study, only 23/70 (33%) patients with LPLN were affected, 21/70 (30%) patients had MRI signs of LPLN metastases. Thus, the sensitivity and specificity of MRI for metastatic lesion of LPLN after CRT were 91% (95% CI: 72.0% — 98.9%) and 38% (95% CI: 24.5%-53.6%), respectively (Table 2). The median size of the short axis of the LPLN in patients with metastatic lesion was 9.2 (7.8; 11.3) mm, whereas in patients without signs of metastasis, the median size was 5.4 (4.2; 6.5) mm ($p < 0.001$).

The operation time was 210 (170; 265) minutes, and the total blood loss was 60 (30;120) ml. Postoperative morbidity developed in 16/70 (23%) patients. All complications corresponded to grade I-II according to Clavien-Dindo's classification and did not require re-operation (Table 3).

The hospital stay was 12 (10;16) days. The follow-up was 14 (8; 20) months. During follow up, 12/70 (16%) patients showed recurrence. Pelvic relapse developed in 3/70 (4%) patients. Distant relapse

Table 2. *Diagnostic accuracy of MRI for detecting metastases in lateral pelvic lymph nodes*

	MRI Metastases (+)	MRI Metastases (–)	Total histology
Metastases have been confirmed	21	2	23
Metastases have not been confirmed	29	18	47

Table 3. *Postoperative morbidity*

Postoperative morbidity	Severity of the morbidity (as per Clavien-Dindo)	Total patients N = 70 n (%)
Anastomotic leakage	II	5/43 (11.6%)
Neurogenic bladder dysfunction [a]	II	5 (7%)
Atonic bladder [b]	II	1 (1.4%)
Post-op ileus	II	5 (7%)
Pelvic hematoma	I	2 (3%)
Lymphedema of the lower limb	I	2 (3%)
Partial loss of sensation and partial impairment of motor activity in the left lower limb	I	1 (2%)
Suture failure of the perineal wound	II	1/23 (4.3%)
Posthemorrhagic anemia [c]	II	1 (1.4%)
Superficial infection of the perineal wound [d]	II	2/23 (8.7%)

Note: a and b, c and d — a combination of complications occurred in 1 patient

was detected in 3/70 (4%) patients in the liver, in 4/70 (6%) patients in the lungs, and in 1/70 (1%) patient in the pelvic bones.

Local recurrences had different anatomical localization and character. In one patient who had previously undergone left LPLD, a recurrence developed on the left side wall of the pelvis involving the levators, ischio-anal tissue, and perineal skin. The recurrence was of an extranodal nature, which may indicate a local microscopic tumor spread beyond the standard dissection margins.

In another patient, an extra-intestinal recurrence was also detected on the left lateral wall of the pelvis with levator involvement without signs of metastatic lymph node lesion, which probably reflects invasive growth or regional lymphogenic spread of the tumor outside the surgical area. The third patient, who had previously undergone right LPLD, had a recurrence in the left obturatory lymph nodes, the contralaterally operated side. These recurrences occurred in the pelvic lymph nodes, which were small in size and were not considered metastatically affected according to the MRI.

DISCUSSION

The lateral lymph nodes is a frequent site for local recurrences of rectal cancer [9]. In a study by Ishihara et al., it was shown that increased LPLN is not an independent prognostic factor of survival, but it is associated with a higher risk of locoregional recurrences, so the 5-year overall survival rate did not differ between patients who had LPLN metastases after CRT and those who had enlarged lymph nodes absent — 81.2% vs. 84.9%, $p = 0.46$ [10]. In a study by Toda et al., out of 92 patients who underwent LPLD, 4 (4%) patients had a local recurrence: two patients had on the dissection side and 2patients had a contralateral one [11]. The combination of LPLD with CRT can be effective locoregional recurrences control, since CRT affects micrometastases and reduces the volume of affected lymph nodes, while LPLD allows radical removal of foci resistant to CRT. According to various studies, LPLD is associated with an increase in intraoperative blood loss and the surgery duration. In the present study, the median blood loss and the median operation time were 60 (30; 120) ml and 210 (170; 265) min, respectively. Only 1 patient had a total volume of blood loss exceeding 800 ml, as, in addition to the left-sided LPLD, he underwent combined abdominal-perineal excision with resection of the left internal iliac artery. Furuhata et al. performed laparoscopic TME with bilateral LPLD in 18 patients with low rectal cancer, while the median blood loss was 105 (5–760)

ml, the median surgery time was 531 (372–682) minutes, and the postoperative hospital stay was 25.5 (9–56) days [12]. The variation in values can be explained by a number of factors. In the study by Furuhata et al., bilateral laparoscopic LPLD prevailed, which is technically more difficult and time-consuming compared to unilateral dissection, which was performed in 64% of cases in this study. In addition, 43% of procedures were open, which reduces the operation time.

Differences in postoperative cure and discharge criteria could also contribute to a shorter hospital stay in this study.

LPLD is associated with an increased risk of postoperative complications such as lymphorrhea, lymphocele, lymphedema of the lower limbs, wound infection, pelvic abscess, and urinary disorders [13–16]. According to a systematic review and meta-analysis by Cormier et al., the incidence of lymphedema reached 22% during pelvic lymphodissection, and 31% after neoadjuvant chemoradiotherapy [17].

Postoperative morbidity in the present study developed in 23 (36%) patients, two patients had a combination of two complications. During the follow-up, no complications of Clavien-Dindo grade III or higher were noted. Five (7%) patients had neurogenic bladder dysfunction. In the study by Furuhata et al., the overall incidence of postoperative complications was 16.7% (3/18), while all complications were also represented by urinary retention, which required repeated catheterization of the bladder and were classified as grade II according to Clavien-Dindo [12]. According to Konishi et al., after laparoscopic TME with LPLD and preoperative CRT none of 14 patients had neurogenic bladder dysfunction [18]. In the study by Tokuhara et al., neurogenic bladder dysfunction developed in 7/38 (18%) patients [19]. Mechanical damage of nerves and plexuses, ischemia due to devascularization, as well as postoperative edema and inflammation in this area during LPLD may play a definite role. It is worth noting that in the presented study, complications such as lymphedema and partial loss of sensitivity and motor activity of the left lower limb developed in two (3%) and one (1.5%) patient, respectively.

In a retrospective single-center study by Mathew et al., lower limb lymphedema developed in the early postoperative period in 3/183 (2%) patients (as per Clavien-Dindo I-II) [20]. These postoperative complications after LPLD may be related to the technical complexity of the procedure, the volume of dissection, previous radiation therapy, and individual anatomical features of patients. The present study, despite the results obtained, has a number of methodological and practical limitations that must be taken into account when interpreting the data. The single-center nature of the study and the limited sample reduce the representativeness of the results, which does not allow them to be fully extrapolated to a wider population. In addition, the relatively short follow-up period limits the ability to reliably assess long-term cancer outcomes, such as overall and disease-free survival. An important factor is also the absence of a control group, which makes it impossible to make a direct comparison with alternative treatment methods, for example, with complete mesorectumectomy without selective lymph dissection. Finally, despite the standardized surgical protocol, the potential variability of TME and LPLD between operating surgeons could affect the final results.

CONCLUSION

Selective LPLD with TME after neoadjuvant treatment seems to be a reasonable option in the treatment of colorectal cancer in cases of suspected LPLN lesion to control local recurrence. However, its role in improving of late outcomes requires additional study in larger-scale and methodologically rigorous clinical trials.

AUTHORS CONTRIBUTION

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