

Initial clinical experience with laparoscopic lateral pelvic lymph node dissection (lymphadenectomy) for advanced low rectal cancer

Le Van Quoc, Ho Huu An,
Diem Dang Binh, Trieu Trieu Duong

108 Military Central Hospital

Summary

Objective: To assess the feasibility, safe, effectiveness of laparoscopic lateral pelvic lymph node dissection (LPLD) for treatment in low rectal cancer. **Subject and method:** This was a prospective cohort study of rectal cancers for multidisciplinary treatment with LPLD at Department of Colon and Rectal Surgery, 108 Military Central Hospital between July 2018 and July 2019. **Result:** Eight patients undergoing LPLD, which were bilateral lymphadenectomy in 3 patients and unilateral lymphadenectomy in 5 patients. There was 4 men and 4 women, with a mean (s.d) age of 56.5 (6.3) years. The median tumour distance from the anal verge was 4.7 ± 1.2 cm (100% the tumor was extraperitoneal - between the peritoneal reflection and the anus). Pre-operative stage was 75% T₄; 25% T₃, 100% N₊. 6 patients underwent preoperative long-course chemoradiation. The mean operation time was 171.2 minutes (range, 140 - 200 minutes), mean operation blood loss was 88.1ml (range, 35 to 200ml). Pre-operative, postoperative morbidity: Hemorrhage was presented as damaged internal iliac veins in 1 patient, 1 patient had anastomotic stenosis. The mean number of harvested lymph nodes was 10.6. The rate of positive lateral lymph nodes was 12.5%. Postoperative cancer stage was 12.5% T₄, 12.5% T₃, 62.5% T₂, 12.5% T₁, 12.5% N₁. The peri-operative and post-operative results of autonomic nerve preservation were performed by using a standard questionnaires of the International Prostate Symptom Score and International Index of Erectile Function. **Conclusion:** The LPLD technique is feasible, safety, effective method for treatment in low rectal cancer.

Keywords: Lateral pelvic lymph node, rectal cancer.

1. Background

The goals of surgery for rectal cancer are to achieve curative resection and maintain quality of life while minimizing the risk of local recurrence and prolonging patient survival time. Lateral pelvic lymph node metastasis was present in 13.9 - 25.5% of patients with lower rectal cancer and that the risk of pelvic recurrence would decrease by 50% and the 5-year survival rate would improve by 8% when lymph node dissection (LLD) was performed for T₃ or

T₄ lower rectal cancer [1]. The standard treatment for locally advanced rectal cancer in Japan is TME with lateral pelvic LLD [2]. In contrast, total mesorectal excision (TME) has been reported to reduce the local recurrence rate and is used with chemoradiotherapy (CRT) as the standard treatment for advanced rectal cancer in Western countries. LPLD has several disadvantages such as prolonged operative time, massive blood loss, and sexual dysfunction. Thus, to avoid overtreatment and morbidity, knowledge of the optimal indications for LPLD in patients with advanced low-rectal cancer treated with preoperative CRT is essential [3].

Correspondence to: Le Van Quoc, Department of Colon and Rectal Surgery, 108 Military Central Hospital

Email: levanquocv108@gmail.com.

Up to now, it has not published any studies of the laparoscopic lateral pelvic lymph node dissection for treatment in low rectal cancer. Therefore, we performed the study this on the purposes: *To assess the feasible, safety, effective LPLD for treatment in low rectal cancer.*

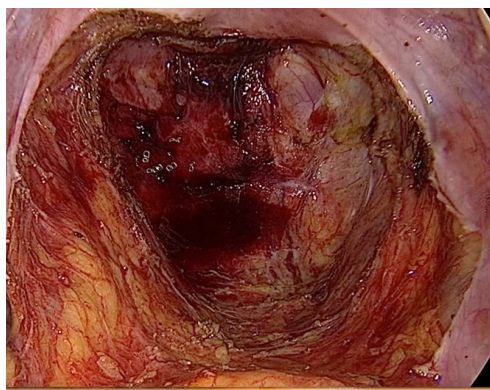
2. Subject and method

2.1. Subject

The prospectively collected records of 8 consecutive patients with low rectal cancer (below the peritoneal reflection) who underwent laparoscopic TME and LPLD in Department of Colon and Rectal Surgery, 108 Military Central Hospital between July 2018 and July 2019. Preoperative staging was performed using digital examination, colonoscopy, and MRI 3.0 Tesla. Radiation (total, 50.4Gy in 28 fractions) with concomitant fluorouracil-based chemotherapy was administered. All these patients had radiologically diagnosed pelvic lymph node metastasis. Lateral pelvic lymph nodes with a diameter of $\geq 7\text{mm}$ before chemoradiotherapy were selectively dissected. Following neoadjuvant treatment, patients underwent repeat staging with MRI before surgery at 6 - 8 weeks after the completion of radiotherapy.

Patient demographics, underlying disease, surgical data, short-term postoperative outcomes including complications, postoperative functional outcomes such as genitourinary function by IPSS (International Prostate Symptom Score) and IIEF (International Index of Erectile Function); data on local and systemic recurrence were analyzed.

2.2. Method



This is prospective, cross-sectional and descriptive study.

The surgical procedures consisted of a low anterior resection, intersphincteric resection which were performed by laparoscopic surgery. All of the procedures included lymphadenectomy using a standard TME technique.

Surgical techniques: Lateral pelvic lymph node dissection preferably should be performed after total mesorectal excision (TME) has been completed and before final primary anastomosis.

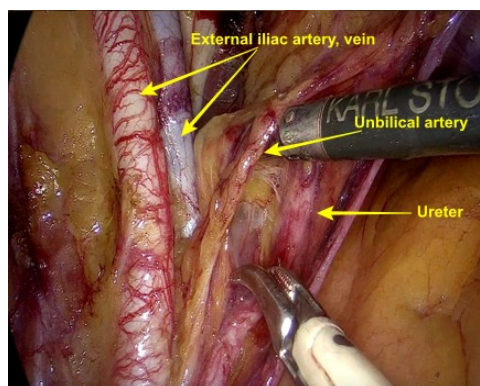
Lateral pelvic lymph node dissection does not require additional trocars. In general, 4 working trocars in addition to the camera trocar are sufficient. The left-sided compartment is usually best approached from the right side by the surgeon. The right-sided compartment may be approached from the left side by the surgeon in its early steps and then from the right side for its most distal part of dissection.

Step 1: Ureter dissection and traction: Tape and separate the ureter and hypogastric nerve to determine the inner edge of the dissection.

Step 2: Lateral border of lateral pelvic lymph node dissection. The external iliac artery is the outer edge of the lateral pelvic lymph node dissection.

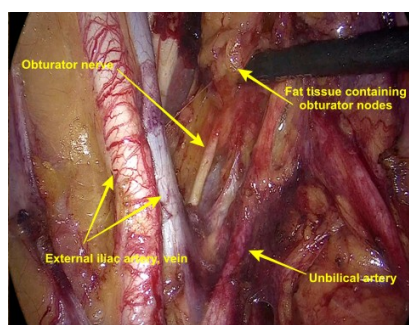
Step 3: Exposure of the obturator foramen. In obturator lymph node dissection, the obturator foramen is confirmed at the caudal end, and the obturator artery/vein is usually separated for dissection.

Step 4: Dissection of the internal iliac nodes. Dissect the lymph nodes in line with the internal iliac artery to the part where the internal pudendal artery enters the pudendal canal.

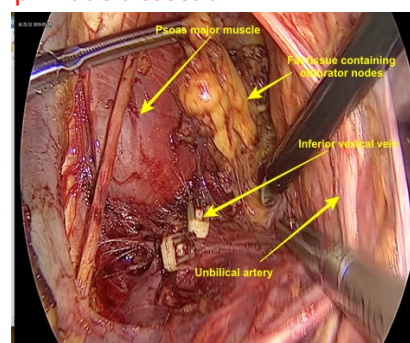


After TME

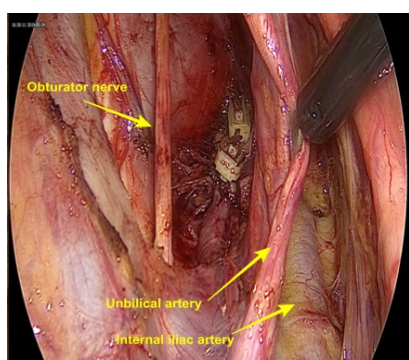
Dissection of the common, internal, external iliac nodes

Figure 1. Procedure for lateral pelvic lymph node dissection

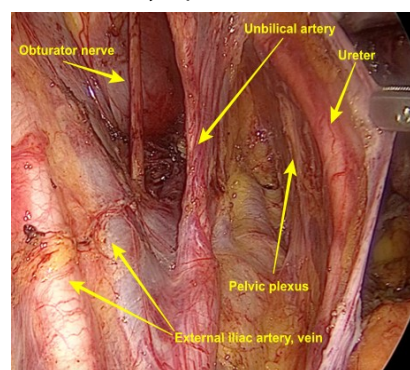
Fat tissue containing obturator nodes



Obturator lymph node dissection



Completion of left lateral pelvic lymph node dissection



Pelvic autonomic nerve preservation

Figure 1. Procedure for lateral pelvic lymph node dissection*(Source: Patient Đinh Văn Đ. 51 years old)*

2.3. Statistical analysis

All statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA).

3. Result

Patient characteristics and operative findings

Table 1. Patient characteristics and operative findings

Characteristics	Case no.	1	2	3	4	5	6	7	8
Age		56	59	51	63	56	67	51	49
Sex		M	M	M	F	M	F	F	F
ASA		1	1	1	2	1	2	1	1
Distance from AV (cm)		3	5	5	5	5	4	7	4
cTNM0		T ₄ N ₁	T ₃ N ₁	T ₄ N ₁	T ₃ N ₂	T ₄ N ₁	T ₄ N ₁	T ₄ N ₁	T ₄ N ₁
Preop. CRT		Yes	Yes	Yes	No	Yes	Yes	No	Yes
Surgical procedure		ISR/ left	ISR/ left	ISR/ both	ISR/ right	ISR/ right	ISR/ both	LAR/ both	ISR/ left
Total OP (min)		180	150	200	140	170	200	180	150
Time for LPLD (min)		30	30	60	20	30	55	50	20
Blood loss (ml)		200	100	50	35	120	50	50	100

ASA: American Society of Anesthesiologists; Preop CRT: Preoperative chemoradiation therapy; OP: Operative; LPLD: Lateral pelvic lymph node dissection; ISR: Intersphincteric resection; LAR: Low anterior resection. AV: Anal verge.

Table 2. Postoperative and pathologic outcomes

Case no.	1	2	3	4	5	6	7	8
Characteristics								
Hospital (day)	15	7	15	6	17	8	7	12
Complication	1	0	0	0	0	0	0	1
No. of lymph nodes harvested	12	6	13	8	12	7	14	13
No. of retrieved LPLN	8	3	5	3	5	3	7	7
No. of positive LPLN	0	0	0	0	0	0	3	0
ypTNM*	T ₂ N ₀	T ₂ N ₀	T ₁ N ₀	T ₂ N ₀	T ₂ N ₀	T ₂ N ₀	T ₄ N ₁	T ₃ N ₀

LPLN: Lateral pelvic lymph node; TNM: Tumor - node - metastasis.

*According to the seventh edition of the American Joint Committee on Cancer staging.

4. Discussion

4.1. Patient characteristics, indications for LPLD

Sugihara et al. retrospectively gathered data from rectal cancer cases at multiple facilities in Japan and reported on the status of LPLN metastasis [1]. Of 1977 cases in which curative surgery had been performed, lateral dissection was performed in 930 patients (47%), with LPLN metastasis confirmed in 129 (13.9%) of the cases undergoing LPLN dissection. The frequency of LPLN metastasis has been reported elsewhere as between 10.6% and 25.5%, with most reports suggesting it is somewhere around 15% [1], [4]. When the tumor location was studied, LPLN metastasis was found in 8.2% of cases when the tumor was intraperitoneal (proximal to the peritoneal reflection) (the upper rectum, defined as Ra in the Japanese classification), but that in 14.9% of cases - a significantly higher rate - when the tumor was extraperitoneal (between the peritoneal reflection and the anus) (the lower rectum, defined as Rb in the Japanese classification) [2], [5]. Kanemitsu et al (2017) studied the tumor location in terms of its distance from the anal verge, demonstrating that in cases where distance from the anal verge was over 9cm, the frequency of LPLN

metastasis was low, at 1.4%, while in cases where it was 9cm or smaller, the rate of metastasis suddenly increased (to 9.1% between 8.1 and 9.0cm, 12.5% between 6.1 and 8.0cm, 20.3% between 4.1 and 6.0cm, 18.8% between 2.1 and 4.0cm, and 23.3% between 0.0 and 2.0cm). An analysis of the depth of tumor invasion by Sugihara et al. showed that the frequency of LPLN metastasis was 7.1% in cases T₂ and shallower, but it was significantly higher (16.6%) in cases T₃ or deeper [1]. Based on this analysis of metastasis frequency, the indication criteria for LPLN dissection according to Japan's Colorectal Cancer Treatment Guidelines were set as "cases in which the lower border of the tumor is located distal to the peritoneal reflection and the tumor has invaded beyond the muscularis propria" [2]. Other risk factors in LPLN metastasis are reported to include being female, histologic types other than well-/moderately differentiated adeno- carcinoma, etc [1].

A retrospective study in 3 centers, 2,263 patients with stage II and III low rectal cancer, including 66 patients with LPLD after preoperation radiotherapy. Analysis of pelvic lymph node metastases and metastatic pelvic results in preoperative radiotherapy response [6]. The results showed that the diameter of lymph nodes before and after chemotherapy greater than 5mm was

significantly related to metastasis rate. Pathological results: The rate of lateral lymph node metastasis in patients with lymph node diameter before and after chemotherapy $\geq 5\text{mm}$ with $< 5\text{mm}$ were 61.1% (22/36 patients) and 0% (0/30 patients, respectively) ($p < 0.001$). Median follow-up time was 39.3 months with the rate of local recurrence in patients with lympho who responded to preoperative treatment was lower than suspected lymph nodes 20% (6/30 patients) and 47.2% (17/36 patients), $p = 0.012$ [7]. In addition, there is a phase III, prospective, multicenter, randomized, single-blind clinical trial recommending pelvic lymph node surgery in patients with low rectal cancer who have suspected lymph node metastasis on MRI (lymph node diameter $\geq 10\text{mm}$, boundary of lymph nodes are not clear, surgery before radiation therapy). Duration of follow-up for 3 years, assessment of relapse rate decreased from 15% to 8%. The trial recommended that pelvic lymph nodes will be a new standard in the treatment of advanced rectal cancer with suspected pelvic lymph node metastases [8].

The Center for selection of patients with low rectal cancer (Rb), with preoperative radiotherapy, with the degree of invasive T_3 , T_4 tumors and suspected lymph node metastases on imaging devices (lymph node diameter: 5mm, 7mm, 8mm or 10mm) [1], [3], [8], [9]. Our research included 4 men and 4 women, with a mean (s.d) age of 56.5 (6.3) years. the median tumour distance from the anal verge was $4.7 \pm 1.2\text{cm}$ (100% the tumor was extraperitoneal - between the peritoneal reflection and the anus). Pre-operative stage was 75% T_4 ; 25% T_3 , 100% N+. All patients with rectal cancer (Rb), suspected lymph nodes metastases on MRI (lymph node diameter $\geq 7\text{mm}$) 6 patients underwent preoperative long - course chemoradiation (total 50.4Gy + capecitabine (Xeloda) 825mg/m²/day). Following neoadjuvant treatment, patients underwent repeat staging with MRI before surgery at 6 - 8 weeks after the completion of radiotherapy (Figure 1).

4.2. Postoperative and pathologic outcomes

Our research included eight patients undergoing LPLD, which was bilateral lymphadenectomy in 3 patients and unilateral lymphadenectomy in 5 patients. Sphincter-preserving rectal cancer surgery was performed in each case and consisted of an intersphincteric resection with coloanal anastomosis for seven patients and a low anterior resection for the remaining one patient. The median operation time was 171.25 ± 22.95 minutes (range, 140 to 200 minutes). The median time for LPLD of one side of the pelvic wall was 36.88 ± 15.80 minutes (range, 20 to 60 minutes). The median blood loss was $88.13 \pm 54.77\text{ml}$ (range, 35 to 200mL). None of the patients needed a blood transfusion during the perioperative period, and the hypogastric nerve, pelvic nerve plexus, and obturator nerve were identified and preserved in all patients. The mean number of harvested lymph nodes was 10.6. The rate of positive lateral lymph nodes was 12.5%. Postoperative stage was 12.5% T_4 ; 12.5% T_3 ; 62.5% T_2 ; 12.5% T_1 ; 12.5% N_1 . The median hospital stay was 10.88 ± 4.39 days (range, 6 to 17 days). The perioperation of the left iliac lymph node surgery, 1 patient suffered an external pelvic vein injury (Tables 1, 2). The average follow-up time of 6.63 ± 2.97 months had 1 patient with anal canal stenosis. Mild disorders of urinary and genital function.

The colorectal cancer study group of the Japan Clinical Oncology Group (JCOG) has also conducted an important multicenter randomized controlled trial comparing mesorectal excision (ME) with or without LLD for clinical stage II or III lower rectal cancer without clinically suspected LLN metastasis (JCOG0212). In total, 701 patients were randomized to the ME with LLND ($n = 351$) and ME alone ($n = 350$) groups. The 5-year relapse-free survival in the ME with LLND and ME alone groups were 73.4% and 73.3%, respectively (hazard ratio: 1.07, 90.9% confidence interval 0.84 - 1.36), with a 1-sided p value for noninferiority of 0.0547. The 5-year overall survival, and 5-year local-recurrence-free survival in the ME with LLND and ME alone groups were 92.6% and 90.2%, and 87.7% and 82.4%, respectively. The numbers of patients with local recurrence were 26

(7.4%) and 44 (12.6%) in the ME with LLND and ME alone groups, respectively ($p=0.024$) [3]. Operation time was significantly longer in the mesorectal excision with lateral lymph node dissection group (median 360 min, IQR 296 - 429) than in the mesorectal excision alone group (254 min, 210 - 307, $p<0.0001$). The lower operation time of our research may be due to the technical level of experienced surgeons, modern equipment and instruments. Blood loss were significantly higher in the mesorectal excision with lateral lymph node dissection group (576mL, IQR 352 - 900) than in the mesorectal excision alone group (337mL, 170 - 566; $p<0.0001$). 26 (7%) patients in the mesorectal excision with lateral lymph node dissection group had lateral pelvic lymph node metastasis. Grade 3 - 4 postoperative complications occurred in 76 (22%) patients in the mesorectal excision with lateral lymph node dissection group and 56 (16%) patients in the mesorectal excision alone group. The most common grade 3 or 4 postoperative complication were anastomotic leakage (18 (6%) patients in the mesorectal excision with lateral lymph node dissection group vs 13 (5%) in the mesorectal excision alone group; $p=0.46$). One patient in the mesorectal excision with lateral lymph node dissection group died of anastomotic leakage followed by sepsis [10]. In the study, we had one patient during the right LPLD, had damaged peritoneal veins causing about 200ml of blood loss, no require blood transfusion and do not transferred open surgery. During follow-up, 1 patient with anorectal stenosis was widened with anal dilator. After that the patient is stable, normal defecation.

5. Conclusion

The LPLD technique is feasible, safety, effective method for treatment in low rectal cancer, less affecting urinary, genital function, more lymph node dredging, the rate of metastatic pelvic lymph nodes 12.5%. However, it is necessary to study more patients and longer follow-up times to evaluate the effectiveness of oncology and quality of life of patients.

References

1. Sugihara K, Kobayashi H, Kato T et al (2006) *Indication and benefit of pelvic sidewall dissection for rectal cancer*. Diseases of the Colon & Rectum 49(11): 1663-1672.
2. Hashiguchi Y, Muro K, Saito Y et al (2019) *Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer*. Int J Clin Oncol.
3. Fujita S, Mizusawa J, Kanemitsu Y et al (2017) *Mesorectal excision with or without lateral lymph node dissection for clinical stage II/III lower rectal cancer (JCOG0212): A multicenter, randomized controlled. Noninferiority Trial*. Annals of Surgery 266(2): 201-207.
4. Mori T, Takahashi K, and Yasuno M (1998) *Radical resection with autonomic nerve preservation and lymph node dissection techniques in lower rectal cancer surgery and its results: The impact of lateral lymph node dissection*. Langenbecks Arch Surg 383(6): 409-415.
5. Japanese Society for Cancer of the Colon and Rectum (2013) *Japanese classification of colorectal carcinoma, 8th edn*. Kanehara & Co.Ltd, Tokyo.
6. Akiyoshi T, Watanabe T, Miyata S et al (2012) *Results of a Japanese nationwide multi-institutional study on lateral pelvic lymph node metastasis in low rectal cancer: Is It regional or distant disease?*. Annals of Surgery 255(6): 1129-1134.
7. Oh HK, Kang SB, Lee SM et al (2014) *Neoadjuvant chemoradiotherapy affects the indications for lateral pelvic node dissection in mid/low rectal cancer with clinically suspected lateral node involvement: A multicenter retrospective cohort study*. Annals of Surgical Oncology 21(7): 2280-2287.
8. Wei M, Wu Q, Fan C et al (2016) *Lateral pelvic lymph node dissection after neoadjuvant chemoradiation for preoperative enlarged lateral nodes in advanced low rectal cancer: Study protocol for a randomized controlled trial*. Trials 17(1): 561.
9. Akiyoshi T, Matsueda K, Hiratsuka M et al (2015) *Indications for lateral pelvic lymph node dissection based on magnetic resonance imaging*

before and after preoperative chemoradiotherapy in patients with advanced low-rectal cancer. Annals of Surgical Oncology 22(S3): 614-620.

10. Fujita S, Akasu T, Mizusawa J et al (2012) *Postoperative morbidity and mortality after mesorectal excision with and without lateral lymph node dissection for clinical stage II or stage III lower rectal cancer (JCOG0212): results from a multicentre, randomised controlled, non-inferiority trial. The Lancet Oncology 13(6): 616-621.*