

Clinical and Oncological Outcomes of Laparoscopic Lateral Pelvic Lymph Node Dissection in Advanced Lower Rectal Cancer: Single-institution Experience

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Abstract. *Aim: The aim of this study was to compare the clinical outcomes of laparoscopic versus open surgery for total mesorectal excision (TME) with lateral pelvic lymph node dissection (LPLD) in advanced lower rectal cancer. Patients and Methods: Forty-four patients who underwent TME with LPLD for lower rectal cancer (pStage II/III) between January 2008 and December 2014 were divided into two groups according to the type of surgical approach as follows: open LPLD group (OLD, n=17) and laparoscopic LPLD group (LLD, n=27). Results: Operative time was comparable between the groups (p=0.15), whereas intraoperative blood loss and complication rates were significantly less in LLD than in OLD. Postoperative hospital stay was shorter in LLD than in OLD. Overall survival and local recurrence-free survival were similar in the two groups. Disease-free survival was better in LLD than in OLD, although the difference was not significant. Conclusion: Laparoscopic TME with LPLD is safe and feasible.*

Rectal cancer is the third most common cancer and the fourth leading cause of cancer-related death worldwide (1). Locoregional recurrence after curative surgery is common in patients with rectal cancer, and is not only a poor prognostic factor, but also a threat to patients' quality of life. Increasing evidence has demonstrated that lateral pelvic lymph node (LPLN) metastasis is a major cause of local recurrence of advanced rectal cancer (2).

In the treatment strategy for LPLN metastases, lateral pelvic lymph node dissection (LPLD) is a point of

controversy between Western countries and Japan. Especially in advanced lower rectal cancer, total mesorectal excision (TME) with neoadjuvant chemoradiotherapy is the standard treatment in Western countries, whereas the Japanese Society for Cancer of the Colon and Rectum guidelines for the treatment of colorectal cancer recommend TME with LPLD (3-5).

Laparoscopic surgery has several advantages over open surgery (6, 7). Laparoscopic colon resection has become widely accepted as a minimally-invasive procedure, with oncological outcomes equivalent to those of open surgery. However, colon surgery, especially for lower rectal cancer, is a complicated technique, and requires a significantly longer operative time and involves more blood loss than TME alone (7). Therefore, most applications of laparoscopic LPLD are still considered investigational in Japan. Although some randomized trials for advanced rectal cancer surgery have demonstrated that laparoscopic surgery provides oncological outcomes equivalent to those of open surgery (8, 9), there are still few reports of laparoscopic TME with LPLD (10-12)

The present study was conducted to assess the efficacy and safety of laparoscopic TME with LPLD compared to the open approach for lower rectal cancer.

Patients and Methods

A total of 57 patients with pathologically proven, pStage II/III lower rectal cancer underwent TME with LPLD for advanced lower rectal cancer at the Nagasaki Medical Center between January 2008 and December 2014. After excluding 12 patients with remote metastases and one with pStage I cancer, 44 patients between were divided into two groups according to the type of surgical approach as follows: open LPLD group (OLD, n=17) and laparoscopic LPLD group (LLD, n=27). Lymph node metastasis was considered present when multidetector computed tomography or magnetic resonance imaging showed lymph node swelling ≥ 5 mm in the short-axis diameter. Dissection of LPLN was performed on the side on which the lymph node swelling was seen. The range of LPLD consisted of three areas (common iliac, obturator, and internal iliac areas).

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In patients with clinical T4Nx or huge tumor spread near the anal canal, neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy was performed based on the decision of a multidisciplinary team conference. The operative approach, either laparoscopic or open, was decided at the surgeon's discretion considering tumor characteristics and the patient's preference. All surgeries were performed by four experienced surgeons. In particular, laparoscopic surgery was performed by trained surgeons with wide experience in laparoscopic surgery of colorectal cancer.

Medical records of all enrolled patients were reviewed retrospectively, including patient characteristics, surgical outcomes, postoperative complications, postoperative hospital stay, and oncological outcomes. These variables were compared between the LLD and OLD groups. *p*-Values of less than 0.05 were considered significant. The chi-squared test (or Fisher's exact test when appropriate) and the Mann-Whitney *U*-test were used for analyses of categorical variables and continuous variables, respectively. Survival endpoints were recorded from the time of surgery and estimated according to the Kaplan-Meier method, and differences between groups were compared by the log-rank test. All study participants provided written, informed consent, and the study design was approved by the Nagasaki Medical Center Ethics Committee (number 28155).

Results

Clinicopathological features of patients. The medical records of 44 patients (27 patients in the LLD group, 17 patients in the OLD group) were reviewed (Table I). No significant difference was found in patient demographics except for the male to female ratio, which was significantly higher in the LLD group. The percentages of patients who received neoadjuvant or adjuvant therapy were also similar between the two groups (Table I). Postoperative pathological findings, including pTNM classification, cell differentiation grade, depth of tumor invasion, and the cancer cell-positive rate of the resection margin were similar between the two groups, whereas the rate of vessel invasion was significantly higher in the OLD group than in the LLD group (Table II).

Operative results. No cases in the LLD group were converted to open surgery. There was no significant difference in the operative time between the groups, while operative blood loss was significantly less in the LLD group than in the OLD group ($p < 0.01$). The rate of sphincter preservation was 77.3% in the LLD group and 52.6% in the OLD group, and the difference was significant ($p < 0.01$). The ratio of unilateral dissection/bilateral dissection was similar in the groups ($p = 0.085$), and the total number of retrieved LPLNs was also not significantly different between the two groups ($p = 0.16$). The rate of TME with *en bloc* resection of the adjacent organ (extended TME) also did not significantly differ between the two groups (Table III).

Surgical complications. Five (18.5%) and 10 (58.8%) patients experienced postoperative complications in the LLD and OLD groups, respectively. The incidence rate was

Table I. Demographics of patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

Parameter	LLD (n=27)	OLD (n=17)	<i>p</i> -Value
Age (years)	64.9	62.4	0.74
Gender (M/F), n	23/4	9/8	0.047
Neoadjuvant therapy, n (%)	5 (18.5%)	1 (5.9%)	0.46
Chemotherapy, n	1	0	
Chemoradiotherapy, n	4	1	
Adjuvant chemotherapy, n (%)	11 (40.7%)	11 (64.7%)	0.12

significantly lower in the LLD group than in the OLD group ($p < 0.01$). There was no perioperative mortality in the two groups. The rates of surgical site infections and anastomotic leakage were similar in the two groups, whereas the rate of urinary incontinence was higher in the OLD group. Postoperative hospital stay was significantly shorter in the LLD group than in the OLD group ($p < 0.01$) (Table IV).

Oncological outcomes. Short-term follow-up was carried out. Median follow-up was 34 months (range=5-53 months) for the LLD group and 60 months (range=9-66 months) for the OLD group. Neither wound nor port-site recurrence was detected in the two groups. OS and LRFS were similar for the two groups. DFS was better for the LLD group than for the OLD group, but the difference was not significant. In the LLD and OLD groups, 3-year OS was 88.9% and 70.1% ($p = 0.38$), 3-year LRFS was 89.5% and 82.4% ($p = 0.35$), and 3-year DFS was 74.7% and 52.9% ($p = 0.098$), respectively (Figures 1-3).

Discussion

The treatment strategy for LPLN metastasis is controversial, especially in advanced lower rectal cancer. In Western countries, metastasis to LPLNs has been regarded as a systemic disease. The standard treatment for locally advanced lower rectal cancer is TME with preoperative radiotherapy or chemoradiotherapy, whereas LPLD is not considered the standard treatment for lower rectal cancer. In addition, it is cited as a reason for a longer operative time, greater blood loss, and postoperative urinary and sexual dysfunction (13). On the other hand, Japanese surgeons generally consider metastasis to LPLNs to be a regional disease, and TME with LPLD is the standard operation for locally advanced lower rectal cancer (14, 15). Akiyoshi *et al.* reported that patients with LPLN metastasis localized to the area of the internal iliac artery had a similar prognosis to N2a cases. Patients with LPLN metastasis other than the area of the internal iliac artery had a poorer prognosis, but the

Table II. Comparison of the pathological parameters in patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

Parameter	Subclass	LLD (n=27)	OLD (n=17)	p-Value
pTNM classification, n	I/II/III	7/5/15	2/3/12	0.27
Differentiation grade, n	Well, mod/poor/muc	21/2/4	13/2/2	0.97
Depth of tumor invasion, n	T2/T3/T4	6/20/1	3/11/3	0.14
Vessel invasion, n	ly 0/1/2/3	6/18/3/0	0/10/5/2	<0.01
	v 0/1/2/3	5/10/10/2	4/4/7/2	0.75
Positive resection margin, n (%)		0 (0)	1 (5.9)	0.81

mod: Moderately differentiated adenocarcinoma, muc: mucinous adenocarcinoma, ly: lymphatic invasion, v: venous invasion.

Table III. Operative results of patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

Characteristic	LLD (n=27)	OLD (n=17)	p-Value
Operative time, min, mean±SD,	356.0±87.3	428.0±133.9	0.15
Operative blood loss, ml, mean±SD	55.0 ±131.9	500.0±884.0	<0.01
Sphincter-preserving surgery, (%)	77.3%	52.6%	<0.01
Pelvic lymph node dissection, n: Uni/bilateral	18/9	11 / 6	0.085
Total number of harvested pelvic lymph nodes	10.0	8.1	0.16
Pelvic organ resection performed, n (%)	5 (18.5%)	3 (17.6%)	0.74

Table IV. Complications experienced by patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

Complication	LLD (n=27)	OLD (n=17)	p-Value
Postoperative complication, n (%)	5 (18.5%)	10 (58.8%)	<0.01
Surgical site infection, n (%)	3 (11.1%)	3 (17.6%)	
Anastomotic leakage, n (%)	2 (7.4%)	3 (17.6%)	
Urinary incontinence, n (%)	0	2 (11.8%)	
Median postoperative hospital stay, days	17.9	31.5	<0.01

prognosis was similar to that of N2b cases and better than that of patients with stage IV disease who underwent curative resection (4). Previous Japanese reports suggested that in advanced lower rectal cancer, TME with LPLD reduced the local recurrence rate by approximately 50% and improved the 5-year survival rate by 8-9% in patients with advanced rectal cancer (6-8).

In the present study, the perioperative results and oncological outcomes were compared between the LLD and OLD groups. The mean surgical time was not significantly different between the groups, whereas the LLD group had significantly less estimated blood loss and a better sphincter-preserving rate. These findings might be attributed to the fact

that the surgeons benefited from the magnified and clear view of laparoscopy in the narrow and deep pelvic cavity, which is advantageous for precise dissection and secure hemostasis. The laparoscopic approach has been reported to take significantly longer than the open approach in some reports (4, 12).

We also recognize the vesicohypogastric fascia as an important landmark in reducing hemorrhage. The vesicohypogastric fascia includes the internal iliac artery as the important landmark for the dissection borders from internal to external areas (16). Identification of the vesicohypogastric fascia at the early operative stage may contribute to less blood loss and shorter operative time.

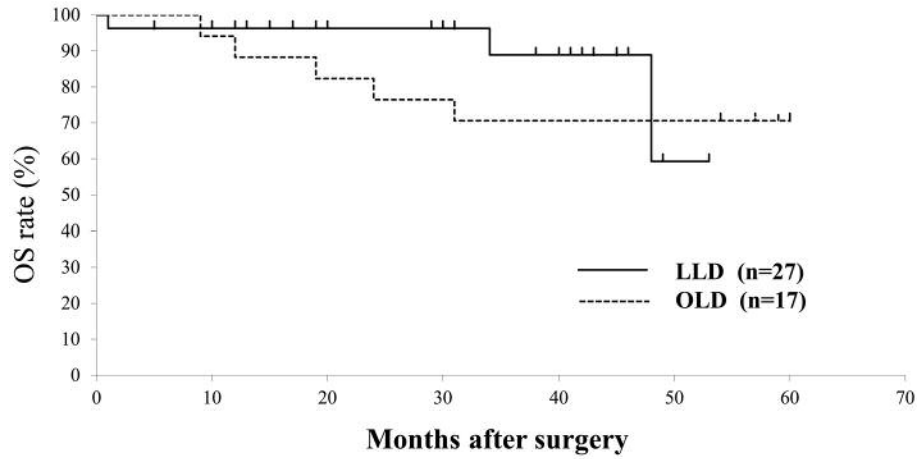


Figure 1. Overall survival (OS) rate of patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

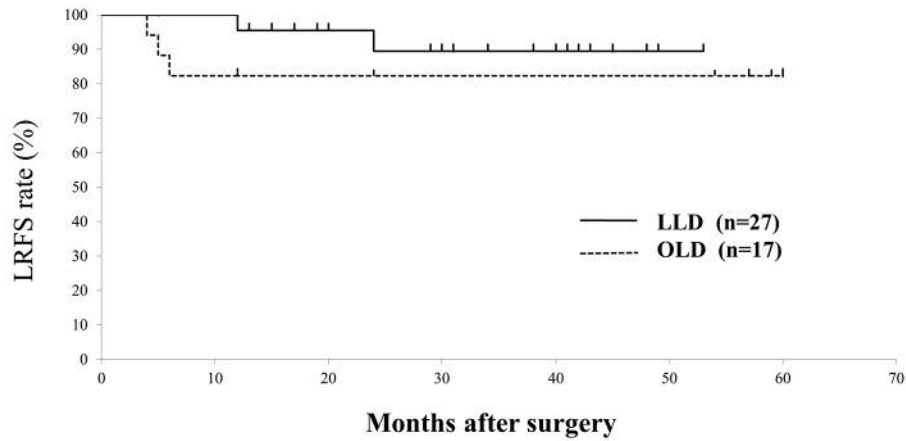


Figure 2. Local recurrence free survival (LRFS) rate of patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

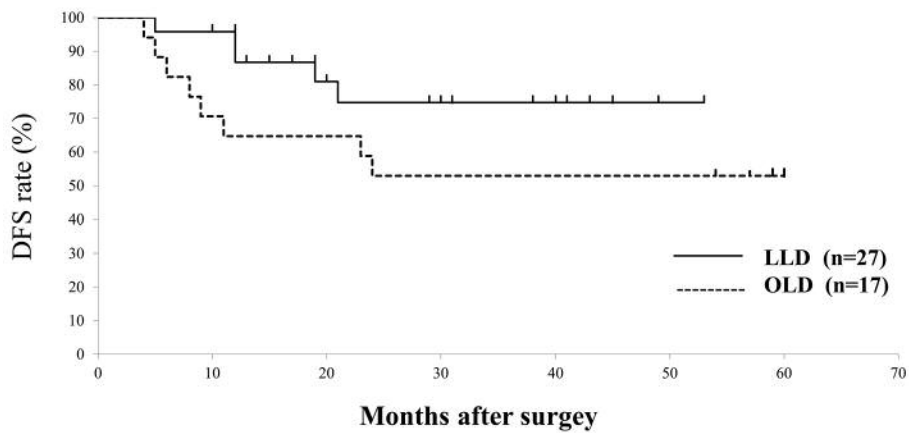


Figure 3. Disease-free survival (DFS) rate of patients who underwent total mesorectal excision with lateral pelvic lymph node dissection by open surgery (OLD) and by laparoscopy (LLD).

It has been reported that the rate of grade 3/4 complications (Clavien-Dindo classification) did not differ significantly between LLD and OLD (4). Yamaguchi *et al.* reported that the rates of wound infection, small bowel obstruction, and anastomotic leakage were lower in a robot-assisted LLD group than in the OLD group (17). In the present study, the rates of postoperative complications were lower in the LLD group. In particular, urinary incontinence occurred only in the OLD group. From the perspective of urinary dysfunction, LLD was superior to OLD in terms of precise dissection and better visualization through the greater magnification of the surgical field, which was advantageous for the preservation of the autonomic nerves. In addition, postoperative hospital stay was significantly shorter in the LLD group because of the lower rate of postoperative complications.

Although some randomized controlled trials for TME with LPLD demonstrated that laparoscopic surgery was not inferior compared to open surgery, there have been few reports of long-term outcomes (18, 19). Nagayoshi *et al.* reported that 3-year OS and 3-year RFS did not differ significantly between LLD and OLD groups (20), consistent with the present results. Akiyoshi *et al.* reported the excellent oncological outcome of patients with LPLN metastasis at their institution and stated that LPLN metastasis can be considered a regional disease amenable to cure with LPLD (21). Laparoscopic surgery is less invasive and useful for an extended operation such as TME with LPLD than open surgery, although it will be necessary to further examine this in the future.

There are several limitations to the present study. Firstly, the limited sample size may have diminished the ability to distinguish the potential difference between the two groups studied. Secondly, this study was a retrospective single-institution study. Lastly, the follow-up period was too short to draw firm conclusions, with a median follow-up of less than 5 years. Future randomized, controlled trials are required to elucidate the oncologic advantage of LLD for advanced lower rectal cancer.

Conclusion

In conclusion, the present study showed that laparoscopic TME with LPLD for advanced rectal cancer is safe and feasible, with an oncological adequacy comparable to that of the open approach. However, this was a retrospective study, and further evidence is necessary to precisely evaluate the laparoscopic surgical and oncological outcomes.

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