Benefit of Lateral Lymph Node Dissection for Rectal Cancer: Long-term Analysis of 944 Cases Undergoing Surgery at a Single Center (1975-2004)

TETSUSHI KINUGASA, YOSHITO AKAGI and KAZUO SHIROUZU

Department of Surgery, Kurume University School of Medicine, Fukuoka, Japan

Abstract. *Background: Pelvic sidewall dissection (PSD) has the potential to decrease local recurrence so that PSD may be an effective strategy for lower rectal cancer. Therefore, it is important to investigate the validity of PSD for its potential clinical use in lower rectal cancer therapy and prognosis. Patients and Methods: The present study included all 994 patients with rectal cancer who underwent curative surgery from January 1975 until December 2004 at the Kurume University Hospital in Fukuoka. The patients were analyzed to determine whether lateral lymph node (LLN) metastasis was correlated with clinicopathological factors, and in the overall study population, 5-year disease-free survival (DFS), and the 5-years overall survival (OS) were analyzed. Results: In patients with stage 3a cancer there was no significant difference in DFS between those with and without PSD. On the other hand, in patients with stage 3b DFS was significantly worse with PSD than without PSD. We analyzed the DFS and OS according to the number of lymph nodes with LLN-positive metastasis. Those with fewer than three positive lymph nodes had a significantly better DFS and OS compared to those with three or more. Moreover, those with only ore region of positive lymph node had a significantly better DFS and OS compared to those with two or more regions. Conclusion: These results demonstrate that PSD was of benefit for prognosis for patients with fewer than three positive lymph nodes, those limited to within only one region and LLN metastasis only.*

Colorectal cancer is the third most common cancer and leading cause of cancer death in Japan, with more than 100,000 new cases and 36,000 deaths per year (1). The most important prognostic factor in colorectal cancer is nodal status, and lymph node metastasis is a determining factor for adjuvant chemotherapy and subsequently key to predicting disease-free (DFS) and overall (OS) survival (2, 3).

Patients with lower rectal cancer have an increased risk of lateral lymph node (LLN) metastasis because the lower rectum drains both upwards through the superior rectal vessels and laterally along the middle rectal vessels and then to the internal iliac vessels. The rates of LLN metastasis in rectal cancer have been reported to range from 8.6% to 29% (4-6). Based on this, pelvic sidewall dissection (PSD) has become a standard procedure for lower rectal cancer in Japan, although it is rarely performed in other countries. One reason that PSD is not performed in other countries may be because positive LLN would represent systemic spread rather than regional disease (7). The standardization of the technique of total mesorectal excision (TME) with accurate dissection of the anatomical plane enveloping the rectum and mesorectum constitutes major progress in rectal cancer surgery. TME has achieved much lower local recurrence rates (8). Moreover, progress in chemoradiotherapy has achieved good local control and better survival rates (9, 10) in many Western countries. These studies have shaped the current Western practice of combining TME with chemo-radiation to achieve good oncological results for rectal cancer. Nevertheless, there are still cases of local recurrence, which is a significant clinical problem that is associated with severe morbidity, a low likelihood of salvage, and eventually death (11).

However, there are some reports that patients with positive LLN can survive for more than five years after PSD. Some reports have shown the five-year survival rates of patients with positive LLN after PSD ranged from 37.3% to 49.3% (12-14), and the survival after PSD in patients with stage 2 disease was significantly better than without PSD (15). These studies have suggested that PSD for LLN-positive cases is an effective procedure in lower rectal cancer, and PSD might reduce local recurrence and improve the five-year survival rate by removal of positive LLNs. Thus, PSD may improve prognosis in pre-selected patients.

Correspondence to: Dr. Tetsushi Kinugasa, Department of Surgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan. Tel: +81 942353311, Fax: +81 942340709, e-mail: kinugasa_tetsushi@med.kurume-u.ac.jp

Key Words: Lateral lymph node dissection, rectal cancer, benefit, pelvic sidewall dissection.

Table I. *Clinicopathological characteristics of patients undergoing pelvic sidewall dissection (n=994).*

	No. of patients	Pelvic side wall dissection, n (A)	Positive lateral lymph node, n (B)	B/A(%)	*p*-Value
Gender					
Male	645	302	39	12.9	0.009
Female	349	148	18	12.1	
Location					
RS+Ra	503	126	12	7.5	0.001
Rb	491	324	47	14.5	
Type of surgery					
AR	110	1	0	0	
LAR	533	212	18	8.4	
Hart	6	1	0	0	
APR	282	235	41	17.4	
Other	63	1	0	0	
Histological grade					
Well	690	295	29	10.9	Well *vs*. non-well,
Mod	223	122	21	17.2	0.0011
Poor	14	10	3	30.0	
Muc	39	23	6	26.0	
Other	28	0	0	0	
Depth of invasion					
T1	134	8	1	12.5	T1+T2 *vs*. T3+T4
T2	180	80	7	8.8	0.3459
T3	403	255	34	12.9	
T4	277	107	17	15.9	
Perirectal lymph node metastasis					
No	543	249	14	5.6	<0.0001
Yes	367	197	45	22.8	
Unknown	81	4	0		
Lymphatic invasion					
No	500	200	15	7.5	<0.0001
Yes	486	248	41	16.5	
Unknown	8	2	1	50.0	
Venous invasion					
No	247	79	7	8.9	0.0002
Yes	736	369	52	14.1	
Unknown	11	2	0	0	

AR: Anterior resection, LAR: low anterior resection, Hart: Hartmann's operation, APR: abdominoperineal resection, Well: well-differentiated adenocarcinoma, Mod: moderately-differentiated adenocarcinoma, Poor: poorly-differentiated adenocarcinoma, Muc: mucinous adenocarcinoma.

We have reported that PSD may be an effective strategy for lower rectal cancer (16). Therefore, it is important to investigate the validity of PSD for its potential clinical use in lower rectal cancer therapy and prognosis. The aim of this study was to investigate the benefit including prognosis for patients who underwent PSD for lower rectal cancer during 1975 to 2004 in our Department.

Patients and Methods

Patient and tissue samples. This study involved all 994 patients with rectal cancer who underwent curative surgery from January 1975 until December 2004 at Kurume University Hospital in Fukuoka, Japan. Informed consent was obtained from each of the patients before performing surgical resection, while also receiving the approval from the Institutional Review Committee for Research on Human Subjects at the Kurume University Hospital (#12135). Clinicopathological factors were assessed according to the tumor node metastasis classification of the International Union Against Cancer (UICC) (17).

Anatomic definition in the pelvic cavity. The rectum was divided into three regions according to the Japanese Classification of Colorectal Carcinoma: rectosigmoid (RS), upper rectum (Ra), and lower rectum (Rb). RS is defined as the region of the rectum between the promontrium and the lower border of the second sacral vertebra, which is equivalent to 12 cm from the anal verge; Ra is located between the lower border of the second sacral vertebra and peritoneal reflection, which is equivalent to 8 cm from the anal verge; and Rb is between peritoneal reflection to the upper border of the anal canal. In this study, we distinguish between the upper

rectum (RS+Ra) and the lower rectum (Rb). The LLN were defined as the lymph nodes located outside the pelvic plexus, along the internal iliac (inside area: I) and common iliac vessels and in the obturator cavity (extra area: E).

Study design and surgical procedures including PSD. PSD was performed based on the preoperative staging by colonoscopy, barium enema examination, computed tomography (CT), or magnetic resonance imaging (MRI). An Rb tumor was a common condition for the indication of PSD when the LLN appeared to be swollen on MRI. Almost all patients underwent bilateral PSD in the early and middle periods (from 1975 to 1994); pre-selected patients underwent selective PSD in the latter period (from 1995 to 2004). In PSD, the fatty and connective tissue outside the pelvic plexus, around the intestinal iliac and common iliac vessels, and in the obturator cavity were removed, resulting in the iliac vessels being skeletonized, with or without pelvic autonomic nerve preservation.

Follow-up and data recording. The follow-up procedures were defined according to the Japanese Consensus Conference on Colon Cancer Management (18). For all surviving patients, follow-up data were obtained during routine clinical care. If the follow-up period lasted more than one year, the data were updated after telephone or mail contact was made with the patient and their personal physician. Where a patient died, the date of death was established after telephone or mail contact, and the cause of death was obtained after examination of medical records and contact with their personal doctor.

End-points. In the overall study population: the 5-year OS and 5-year DFS were analyzed.

Statistical analysis. Statistical analysis was performed using JMP version 10.0 (SAS Institute Inc., Cary. NC, USA). Statistical comparisons were made using Fisher's exact test, the x^2 test, or the Wilcoxon rank-sum test, depending on the type of data. Values of $p<0.05$ were considered to indicate statistical significance. OS was defined as the time between diagnosis and the date of death or last follow-up. Survival distributions were estimated using the adjusted Kaplan–Meier method (inverse probability of treatment weighting) and compared using a log-rank test.

Results

Clinicopathologic characteristics. The clinical characteristics of the patients are summarized in Table I. A total of 994 patients with rectal cancer underwent curative surgery. The tumor was located in the upper rectum (RS and Ra) in 645, and in the lower rectum (Rb) in the other 349. Out of 994 patients, PSD was performed in 450 patients (45.3%); for 126 patients (28.0%) in the upper rectum, and for 324 patients (72.0%) in the lower rectum. Positive LLNs were identified in 59 patients (13.1%); in 12 in the upper rectum, and in 47 in the lower rectum. The rate of positive LLNs among patients who underwent PSD was 7.5% in the upper rectum, and 14.5% in the lower rectum. Because of these findings, the cases involving the upper rectum were excluded from further analysis.

Almost all patients underwent bilateral PSD in the early and middle periods (from 1975 to 1994); pre-selected patients underwent PSD in the latter period (from 1995 to 2004). The patients with LLN metastasis were analyzed according to tumor location, histological grade, depth of invasion, perirectal lymph node metastasis, lymphatic invasion and venous invasion.

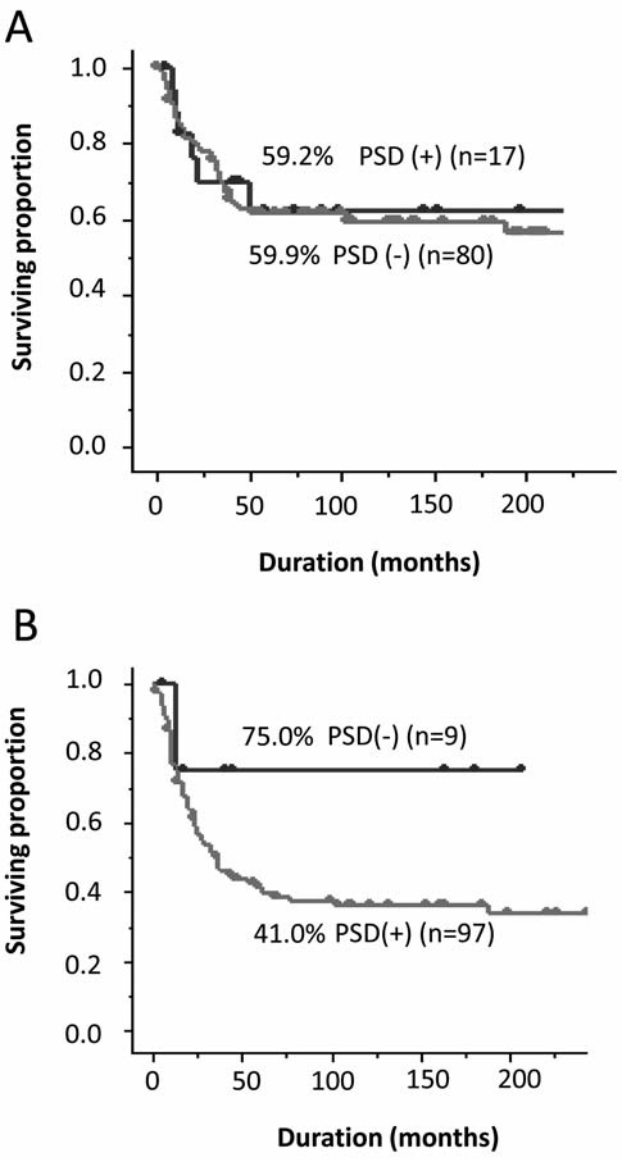

Figure 1. *Kaplan–Meier survival curves of disease-free survival (DFS) at different stages of rectal cancer with (+) and without (–) pelvic side wall dissection (PSD). A: Stage 3a; (+) vs. (–) p=0.914, B: stage 3b; (+) vs. (–) p=0.123.*

Kaplan–Meier OS and DFS curve analysis. In the training set, the average follow-up time for OS was 215.4±36.4 months, and that of DSF was 213.0±34.6 months. Figure 1 shows the DFS at each stage in patients with and without

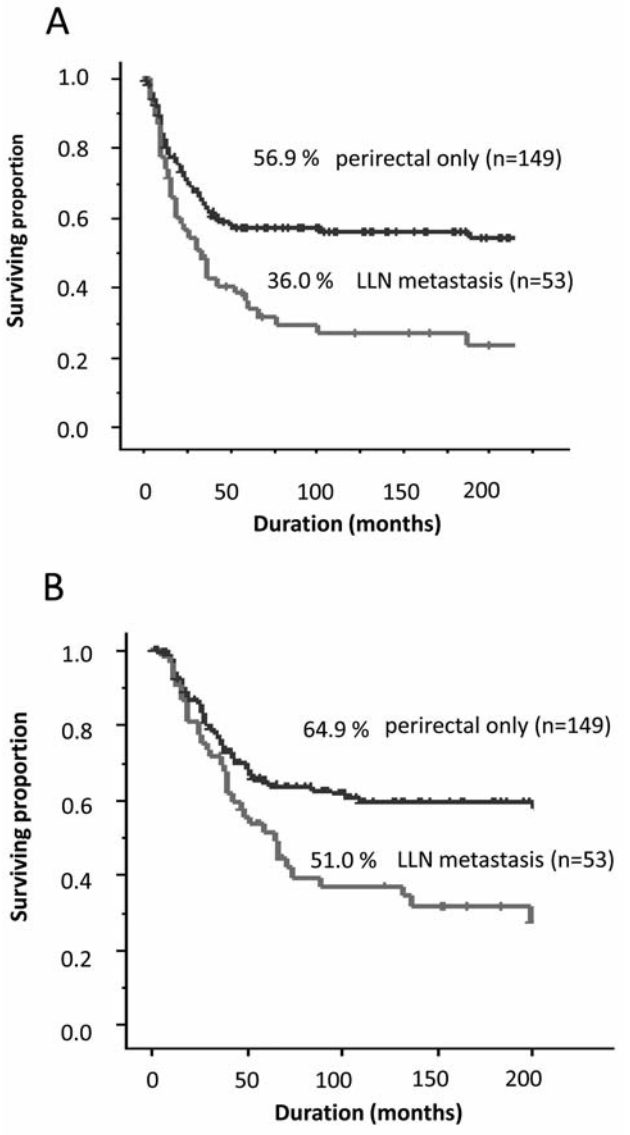

Figure 2. *Kaplan-Meier survival curves of disease-free (DFS) (A) and overall (OS) (B) survival of patients with stage 3a and 3b disease after pelvic side wall dissection (PSD) comparing patients with perirectal lymph node metastasis to those with lateral lymph node (LLN) metastasis. (A); perirectal only vs. LLN metastasis p=0.001, (B); perirectal only vs. LLN metastasis p=0.0043.*

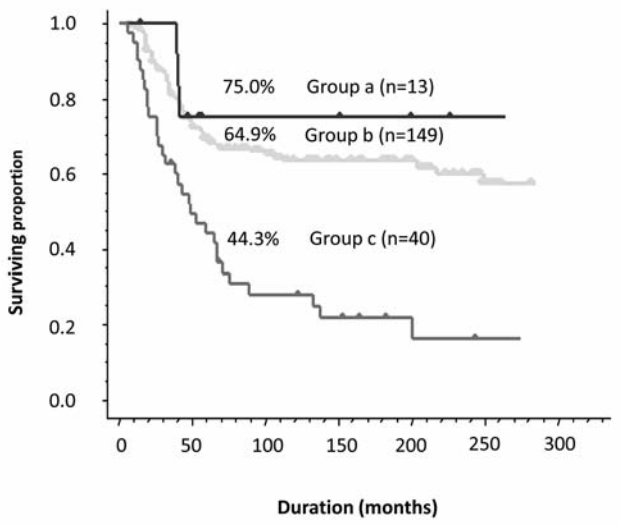

Figure 3. *Kaplan-Meier survival curves of overall survival (OS) after pelvic side wall dissection (PSD) for lower rectal cancer in patients with metastasis only in lateral lymph node (LLN) (Group a), perirectal lymph node metastasis only (Group b), and those with both perirectal lymph node metastasis and LLN metastasis (Group c). Group a vs. Group c, p=0.0081.*

PSD. In patients with stage 3a cancer, there was no significant difference in DFS between those with and those without PSD (Figure 1A). On the other hand, in patients with stage 3b cancer, there was a significant difference in DFS between those with and those without PSD. In patients with stage 3b, DFS was significantly worse in those treated with PSD than in these not (Figure 1B). Figure 2 shows the DFS and OS for patients with stage 3a and 3b cancer with PSD comparing perirectal lymph node metastasis to those with LLN metastasis. In patients with stage 3a and stage 3b cancer, there was a significant difference in DFS with PSD (Figure 2A). Similarly, in patients with the same stage of cancer, there was a significant difference in OS between those with and those without PSD (Figure 2B). In both cases, patients with stage 3b disease who underwent PSD had a worse prognosis than those without PSD.

The five-year OS after PSD in patients with lower rectal cancer is shown in Figure 3. Among those with involved perirectal lymph nodes, 24.5% had positive LLNs. Thirteen patients (5.9%) had positive LLNs without perirectal lymph node metastasis. We divided patients into three groups: (a) those with only LLN metastasis; (b) those with only perirectal lymph node metastasis; and (c) those with both perirectal lymph node metastasis and LLN metastasis. Five-year OS of each group (a, b, and c) was 75.0%, 64.9%, and 44.3%, respectively. In patients with both perirectal lymph node and LLN metastasis, these were significant predictors of reduced OS. On the other hand, the OS was significant better in those with metastasis only in LLNs, than in those with both perirectal lymph node and LLN metastasis.

OS and DFS curve analysis by LLN metastasis. It is important to investigate the validity of PSD for its potential clinical use in lower rectal cancer therapy and prognosis. The purpose of this study was to investigate the benefit including prognosis of the patients who underwent PSD for lower rectal cancer. The median number of dissected LLNs was 23

Table II. *Location of lateral lymph node metastases (N=53).*

Lymph node location	No. of cases
Proximal internal iliac	11
Distal internal iliac	36
External iliac	3
Common iliac lymph node	3
Oburator	17
Middle sacral	1

(range=0-66). Positive LLNs were found in 59 patients (in 13.1% of patients with PSD), and we followed-up 53 patients after surgery. Figure 4 shows the DFS and OS after PSD, comparing patients with fewer than three and those with three or more positive LLNs. Patients with three or more positive LLNs had significantly reduced DFS and OS.

In addition, we analyzed the location of positive LLNs. We divided the area into two parts, area I, and area E. We defined positive LLN located along the internal iliac artery as being in area I (47 patients; 89%), and those around the oburator vessels and nerve as being in area E (17 patients; 32%) (Table II).

Figure 5 shows the DFS and OS after PSD in the patients comparing those with only one area and those with two or more areas of metastasis. Patients with two or more areas of LLN metastasis had a significantly worse DFS and OS.

These results suggest that there is benefit of PSD for lower rectal cancer, including prognosis, of patients with LLN metastasis only, fewer than three positive LLNs, and only one area of metastasis.

Discussion

Patients who underwent PSD for lower rectal cancer with LLN metastasis only, fewer than three positive LLNs, and only one area of metastasis clearly benefited from PSD. In addition, in cases where positive perirectal lymph node metastasis was suggested by CT or MRI, LLN swelling should be evaluated and PSD considered, using touch manipulation during the operation.

The approach to rectal cancer management in Japan differs from that in Western countries in terms of how LLN metastasis is viewed. In Western countries, LLN metastasis is considered to be a systemic disease that should be treated by radiotherapy or chemotherapy (7). The standard treatment for patients with locally advanced rectal cancer is preoperative chemoradiotherapy followed by transabdominal resection based on TME, and local recurrence rates below 10% have been achieved using this method (11). However in Japan, LLN involvement is considered to be a local disease, and thus extensive PSD is performed to reduce local recurrence and improve survival (16).

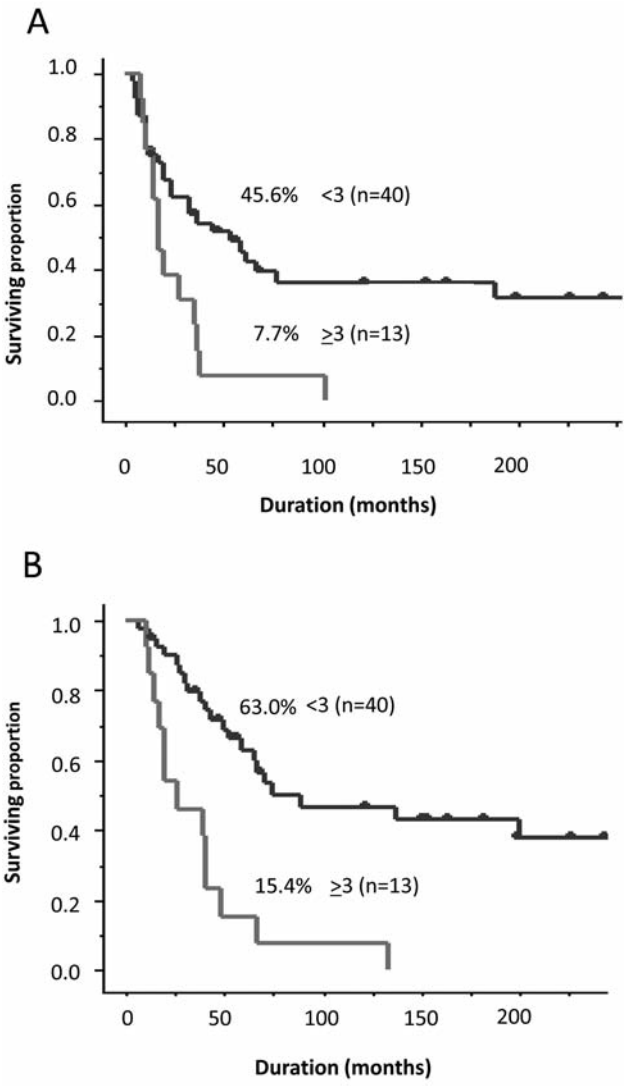

Figure 4. *Kaplan–Meier survival curves of disease-free (DFS) (A) and overall (OS) survival (B) of patients with lateral lymph node (LLN) metastasis after pelvic side wall dissection (PSD) comparing those with fewer than three metastases to those with three or more. (A); <3 vs. ≥3, p=0.0046, (B); <3 vs. ≥3, p=0.0001.*

In the early 1980s, extended PSD was performed without full understanding of the pelvic autonomic innervations, which led to the observation of urinary and sexual dysfunction after surgery in Japan. Since then, attention had been paid to the anatomical conditions and preservation of the pelvic autonomic nerves, which has consequently reduced the incidence of complications after lower rectal surgery. In addition, PSD was performed for pre-selected patients. There remains a need to detect positive LLNs in the pelvic area. The accurate identification and characterization of lymph nodes using imaging has

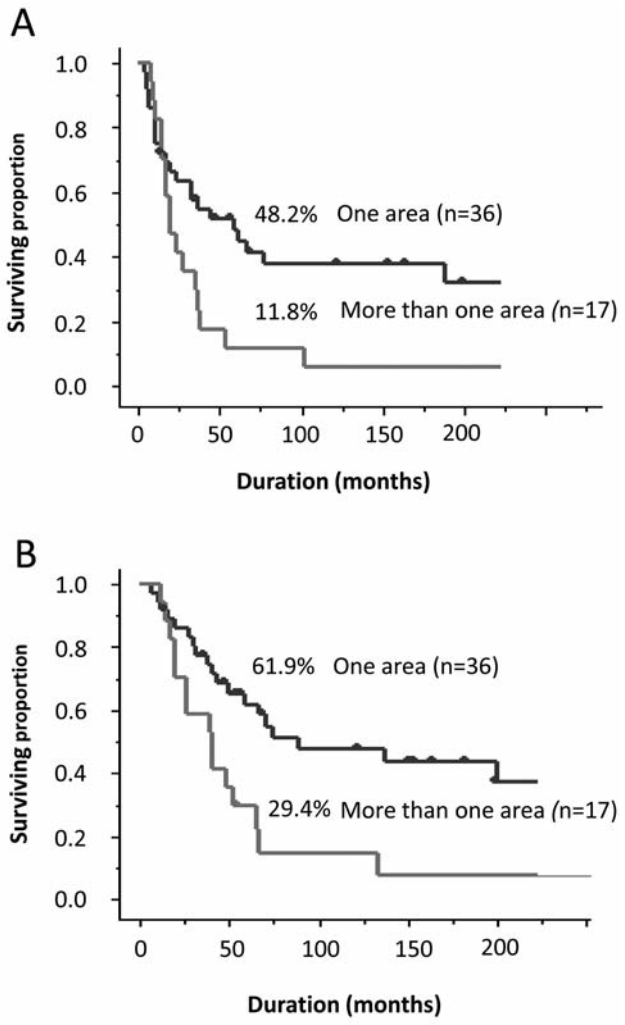

Figure 5. *Kaplan–Meier survival curves of disease-free (DFS) (A) and overall (OS) survival on patients treated with pelvic side wall dissection (PSD) (B) comparing those with lateral lymph node (LLN) metastasis in one area to those in more than one area. (A); one area vs. more than one area p=0.0208, (B); one area vs. more than one area p=0.0048.*

important therapeutic and prognostic significance in patients with lower rectal cancer.

Recently, MRI has become a key diagnostic tool in rectal cancer. In the evaluation of depth of tumor invasion and lymph node metastasis, the diagnostic accuracy of MRI is superior to that of CT (19, 20). Some reports have suggested that a 6-mm longitudinal diameter criterion is optimal in the evaluation of mesorectal lymph node status in patients with rectal cancer (21). Thus pelvic MRI is now usually performed to determine positive LLNs preoperatively. These MRI findings can indicate the need for selective LLN dissection in lower rectal cancer.

We also found a high frequency of positive LLNs in those located along the internal iliac artery and around the oburator vessels and nerve. MRI has become a promising diagnostic tool in rectal cancer for LLN estimation (16).

Various factors such as gender, location, and perirectal lymph node metastasis have been suggested as significant predictors of the presence of positive LLNs. The location, histological grade, and mesenteric node metastasis have been found to be significant predictors of positive LLNs (14). We have previously reported that perirectal lymph node metastasis was the best predictor of positive LLN (16).

The prognostic benefits of PSD are controversial. A meta-analysis comparing extended lymphadenectomy with conventional surgery concluded that lymphadenectomy did not seem to confer a significant overall cancer-specific advantage (22). Japanese surgeons disagree with these conclusions because of the disparate groups that were used in the different studies and the fact that the meta-analysis did not consider the changes made by the Japanese Surgical Society in terms of indication criteria and techniques (23).

The benefit, if any, of TME with PSD over TME-alone for pre-selected patients, with clinical stage II or III low rectal cancer, is under investigation in the Japanese JCOG0212 trial that was started in 2003. This is a multi-center trial randomizing patients with low rectal cancer to TME or TME with PSD. The results of JCOG 0212 will only be available around 2016.

In the present study, LLN metastasis was associated with a poor prognosis and high risk of recurrence. The 5-year DFS and OS rates of patients with LLN metastasis were 36.0% and 51.0%, respectively. There have been many reports on the 5-year survival rates of patients undergoing extended PLD in the presence of metastatic LLNs, ranging from 37.3% to 49.3% (12, 15, 24).

Although the survival rates of the present study cannot be compared to previously reported rates, it is clear that some patients could be treated by selective LLN excision successfully. Naturally, the role of postoperative chemotherapy in extending patient survival should also be considered, but its impact could not be evaluated in the present study.

The new finding in this study is that for patients treated with PSD for LLN metastasis alone, the prognosis is better than for those with only perirectal lymph node metastasis, and better than having both perirectal lymph node and LLN metastasis. Another new finding from this study is that prognosis after PSD was better in those with fewer than three affected LLNs, and in those with only one affected region of LLN.

Although this study was the first to analyze the benefit, the indications and prognostic roles of selective PSD, as a retrospective study, it has certain inherent limitations. Data regarding the exact location and distribution of the retrieved LLNs were not available. Another limitation is that the oncological data are not available for the control group without PSD despite suspicious LLNs. Considering the extension of recent surgical indication of metastatic lower rectal cancer, the role of selective PSD has a reasonable risk. However, because

PSD was not performed in all the included patients, the actual degree of beneficial effect of PSD could not be fully evaluated.

In any event, LLN metastasis in patients with lower rectal cancer undergoing PSD was a distinct factor conferring a poor prognosis. However, selective PSD based on imaging studies may have a good benefit for prognosis in patients with LLN metastasis.

In this study, we demonstrated that the benefit, including of better prognosis, of the patients who underwent PSD for lower rectal cancer was found for those with (i) LLN metastasis only, (ii) fewer than three positive LLN metastases, and (iii) affected LLNs located in only one area. Our current findings suggest that PSD may be considered a good therapeutic strategy for lower rectal cancer. We hope these findings support new efforts for the clinical application of PSD in patients with LLN metastasis with lower rectal cancer.

References

1 Kotake K, Honjo S, Sugihara K, Kato T, Kodaira S, Takahashi T, Yasutomi M, Muto T and Koyama Y: Changes in colorectal cancer during a 20-year period: an extended report from the multi-institutional registry of large bowel cancer. Japan. Dis Colon Rectum *46*: S32-43, 2003.

2 Newland RC, Chapuis PH, Pheils MT and MacPherson JG: The relationship of survival to staging and grading of colorectal carcinoma: a prospective study of 503 cases. Cancer 47: 1424-1429.1981.

3 Chapuis PH, Dent OF, Fisher R, Newland RC, Pheils MT, Smyth E and Colquhoun K: A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. Br J Surg 72: 698-702.1985.

4 Akasu T, Sugihara K, and Moriya Y: Male urinary and sexual functions after mesorectal excision alone or in combination with extended lateral pelvic lymph node dissection for rectal cancer. Ann Surg Oncol *16*: 2779-2786, 2009.

5 Kim TH, Jeong SY, Choi DH, Kim DY, Jung KH, Moon SH, Chang HJ, Lim SB, Choi HS and Park JG: Lateral lymph node metastasis is a major cause of locoregional recurrence in rectal cancer treated with preoperative chemoradiotherapy and curative resection. Ann Surg Oncol *15*: 729-737, 2008.

6 Yano H, Saito Y, Takeshita E, Miyake O and Ishizuka N: Prediction of lateral pelvic node involvement in low rectal cancer by conventional computed tomography. Br J Surg *94*: 1014-1019, 2007.

7 Enker WE, Thaler HT, Cranor ML and Polyak T: Total mesorectal excision in the operative treatment of carcinoma of the rectum. J Am Coll Surg *181*: 335-346, 1995.

8 Heald RJ, Husband EM, and Ryall RD: The mesorectum in rectal cancer surgery – the clue to pelvic recurrence? Br J Surg *69*: 613-616, 1982.

9 Syk E, Glimelius B and Nilsson PJ: Factors influencing local failure in rectal cancer: analysis of 2315 patients from a population-based series. Dis Colon Rectum *53*: 744-752, 2010.

10 Kusters M, Marijnen CA, van de Velde CJ, Rutten HJ, Lahaye MJ, Kim JH, Beets-Tan RG and Beets GL: Patterns of local recurrence in rectal cancer; a study of the Dutch TME trial. Eur J Surg Oncol *36*: 470-476, 2010.

11 Lim SB, Yu CS, Kim CW, Yoon YS, Park SH, Kim TW, Kim JH and Kim JC: Clinical implication of additional selective lateral lymph node excision in patients with locally advanced rectal cancer who underwent preoperative chemoradiotherapy. Int J Colorectal Dis *28*: 1667-1674, 2013.

12 Ueno H, Mochizuki H, Hashiguchi Y and Hase K: Prognostic determinants of patients with lateral nodal involvement by rectal cancer. Ann Surg *234*: 190-197, 2001.

13 Shirouzu K, Ogata Y, Araki Y, Sasatomi T, Nozoe Y, Nakagawa M and Matono K: Total mesorectal excision, lateral lymphadenectomy and autonomic nerve preservation for lower rectal cancer: significance in the long-term follow-up study. Kurume Med J *48*: 307-319, 2001.

14 Ueno M, Oya M, Azekura K, Yamaguchi T and Muto T: Incidence and prognostic significance of lateral lymph node metastasis in patients with advanced low rectal cancer. Br J Surg *92*: 756-763, 2005.

15 Sugihara K, Kobayashi H, Kato T, Mori T, Mochizuki H, Kameoka S, Shirouzu K and Muto T: Indication and benefit of pelvic sidewall dissection for rectal cancer. Dis Colon Rectum *49*: 1663-1672, 2006.

16 Kinugasa T, Akagi Y, Ochi T, Ishibashi Y, Tanaka N, Oka Y, Mizobe T, Yuge K, Fujino S, Kibe S and Shirouzu K: Lateral lymph-node dissection for rectal cancer: meta-analysis of all 944 cases undergoing surgery during 1975-2004. Anticancer Res *33*: 2921-2927, 2013.

17 TNM: classificaation of Malignant Tumours 7th. Edition. L.H. Sobin, M.K. Gospodarowicz and Ch. Wittekind, Backwell Publising Ltd, Oxford, UK, 2009.

18 General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus, Seventh Edition. Kanehara Shuppan, Tokyo, Japan, 2014.

19 Beets-Tan RG, Beets GL, Vliegen RF, Kessels AG, Van Boven H, De Bruine A, von Meyenfeldt MF, Baeten CG and van Engelshoven JM: Accuracy of magnetic resonance imaging in prediction of tumour-free resection margin in rectal cancer surgery. Lancet *357*: 497-504, 2001.

20 Brown G, Richards CJ, Newcombe RG, Dallimore NS, Radcliffe AG, Carey DP, Bourne MW and Williams GT: Rectal carcinoma: thin-section MR imaging for staging in 28 patients. Radiology *211*: 215-222, 1999.

21 Matsuoka H, Nakamura A, Sugiyama M, Hachiya J, Atomi Y and Masaki T: MRI diagnosis of mesorectal lymph node metastasis in patients with rectal carcinoma. what is the optimal criterion? Anticancer Res *24*: 4097-4101, 2004.

22 Georgiou P, Tan E, Gouvas N, Antoniou A, Brown G, Nicholls RJ and Tekkis P: Extended lymphadenectomy versus conventional surgery for rectal cancer: a meta-analysis. Lancet Oncol *10*: 1053-1062, 2009.

23 Yano H, Moran BJ, Watanabe T, and Sugihara K: Lateral pelvic lymph-node dissection: still an option for cure. Lancet Oncol *11*: 114; author reply 114-115, 2010.

24 Sugihara K, Moriya Y, Akasu T, and Fujita S: Pelvic autonomic nerve preservation for patients with rectal carcinoma. Oncologic and functional outcome. Cancer *78*: 1871-1880, 1996.

Received April 4, 2014
Revised June 11, 2014
Accepted June 12, 2014