

Morphological characteristics of lateral pelvic lymph nodes in locally advanced lower rectal cancer: A retrospective study

Yushi Suzuki  | Takeshi Sasaki | Hiro Hasegawa | Koji Ikeda | Koichi Teramura |
Yuichiro Tsukada | Yuji Nishizawa | Masaaki Ito 

Department of Colorectal Surgery,
National Cancer Center Hospital East,
Chiba, Japan

Correspondence

Masaaki Ito, Department of Colorectal
Surgery, National Cancer Center Hospital
East, 6-5-1 Kashiwanoha, Kashiwa, Chiba
277-8577, Japan.
Email: maito@east.ncc.go.jp

Abstract

Aim: This study aimed to investigate the potential of the size and aspect ratio of metastatic and non-metastatic lateral pelvic lymph nodes (LPLNs) as low-risk markers for locally advanced lower rectal cancer, without treatment by neoadjuvant chemoradiation therapy or LPLN dissection.

Methods: This single-center, retrospective cohort study evaluated 310 consecutive patients diagnosed with lower rectal cancer (T: T3/T4, N: any, and M: M0) who underwent curative surgery without neoadjuvant therapies between 2010 and 2018. The harvested LPLNs were categorized into groups A (metastasis-positive lymph nodes), B (metastasis-negative lymph nodes in the area bearing metastasis-positive lymph nodes), C (metastasis-negative lymph nodes in a metastasis-negative area in metastasis-positive patients), and D (lymph nodes in non-metastatic patients). The main outcome measure was the relationship among lymph node size, aspect ratio, and metastasis in the LPLNs.

Results: Overall, 3962 LPLNs were harvested. The long and short axes and the aspect ratio were significantly longer and higher, respectively, in group A than in the other groups ($P < .001$). The aspect ratio in group B was significantly higher than that in groups C and D ($P < .001$). The aspect ratio in group C was significantly higher than that in group D ($P < .001$). Furthermore, no metastasis-positive lymph nodes had an aspect ratio of less than 0.4. Metastasis-positive LPLNs tended to be larger and rounder than their metastasis-negative counterparts.

Conclusions: Metastatic LPLNs in patients with lower rectal cancer are significantly larger and have a higher aspect ratio. Lymph nodes with aspect ratios of <0.4 were metastasis negative.

KEYWORDS

aspect ratio, lateral pelvic lymph node, local recurrence, pathological morphology, rectal cancer

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Authors. *Annals of Gastroenterological Surgery* published by John Wiley & Sons Australia, Ltd on behalf of The Japanese Society of Gastroenterology.

1 | BACKGROUND

Lateral pelvic lymph node (LPLN) metastasis leads to local recurrence of locally advanced lower rectal cancer (LALRC) in the pelvis. Total mesorectal excision (TME) has markedly reduced the local recurrence rate and increased the curative resection rate for LALRC. Furthermore, the introduction of neoadjuvant chemoradiation therapy (NACRT) has improved local control not only in the central pelvic area but also in the lateral pelvic area.¹⁻⁴ However, local recurrence after radical resection for LALRC remains a major problem that affects prognoses and quality of life. Although a combination of NACRT and LPLN dissection (LPLND) is more effective in reducing the incidence of local recurrence, performing both procedures is too invasive in most cases owing to the low rate of LPLN metastases. The JCOG0212 trial (randomized clinical trial: NCT00190541, UMIN-CTR: C000000034) reported that in patients with rectal cancer who underwent TME followed by LPLND when swollen LPLNs were not identified on preoperative imaging, only 7.4% actually presented with LPLN metastases.⁵

A recent study reported that LPLND reduced the local recurrence rate in patients with an LPLN short axis of ≥ 5 mm, even if they had undergone NACRT.⁶ Another study demonstrated a correlation between local recurrence and an LPLN short-axis diameter > 7 mm in patients who received NACRT.⁷ However, there are insufficient data on the optimal methodology for detecting LPLN metastases accurately, irrespective of whether the patients have received NACRT. In general, LPLN metastasis is detected using the diameters of the long and short nodal axes on preoperative magnetic resonance imaging (MRI) or computed tomography (CT).⁸⁻¹² However, although there are existing reports on lymph node metastases of esophageal, biliary, gynecological, and bladder cancers that discuss the nodal aspect ratio on preoperative imaging modalities,¹³⁻¹⁶ there are no reports on the aspect ratio (i.e. the ratio of the short axis diameter to the long axis diameter) of the lymph nodes in LALRC.

Given the importance of addressing the pathomorphological characteristics of LPLN metastases, this study aimed to investigate the potential of the size and aspect ratio of metastatic and non-metastatic LPLNs as low-risk markers for LALRC without treatment by NACRT or LPLND. Towards this goal, data from consecutive patients with LALRC who underwent curative resection of the rectum with LPLND were analyzed. We also analyzed the impact of non-metastatic lymph nodes surrounding the positive LPLN in each lateral pelvic area.

2 | METHODS

2.1 | Study design and patients

This retrospective, single-center study evaluated consecutive patients who were diagnosed with LALRC and underwent curative

elective resection without NACRT and neoadjuvant chemotherapy (NAC) at the National Cancer Center Hospital East (Japan) between January 2010 and December 2018. LALRC was defined as the presence of a tumor (TNM stage; T: T3/T4, N: any, and M: M0) below the second valve of Houston (within 8-10 cm from the anal verge), which corresponds to the position of the peritoneal reflection. From this initial population, patients who did not undergo LPLND after TME or tumor-specific mesorectal excision were excluded. Furthermore, patients who underwent preoperative treatment were also excluded because treatment with NACRT and NAC may have affected the pathomorphological findings on the associations between LPLN and LPLN metastasis. In total, 310 patients who underwent curative resection of c-stage II or III LALRC with LPLND and who did not receive any type of NAC or radiation therapy were evaluated. Data on the patients' age, sex, anal verge distance, clinical TNM classification, clinical circumferential resection margin (cCRM), type of surgery, and pathological findings of the primary tumor were collected for analysis. cCRM positive was defined as when the distance from the tumor or metastasis-positive lymph node to the mesorectal fascia was < 2 mm upon MRI.

2.2 | Variable definition

Rectal resection and LPLND for internal iliac and obturator lesions were performed as previously described.¹⁷ In this study, obturator node metastasis was classified as a regional and not distant metastasis of rectal cancer in accordance with the Japanese guidelines for colorectal cancer.¹⁸ The harvested lymph nodes from the lateral pelvic area were removed from the dissected adipose tissue immediately postoperatively and before formalin fixation. LPLNs were characterized by the presence of internal iliac and obturator lymph nodes on both sides. After formalin fixation and paraffin embedding, the LPLNs were placed at the maximum split surface for pathological examination and stained with hematoxylin and eosin. LPLNs were diagnosed as metastasis positive or metastasis negative according to the presence of metastatic cancer cells. Accordingly, the patients were categorized to have lateral metastasis-positive or lateral metastasis-negative disease.

Figure 1 shows the harvested LPLNs (collected from the dissected adipose tissue) classified into four groups (A, B, C, and D), according to their positional relationship with the metastasis-positive lymph nodes. Group A comprised metastasis-positive LPLNs. Group B comprised metastasis-negative LPLNs in metastasis-positive patients, which were located on the same side and in the same area (i.e. the internal iliac or obturator region) that contained a positive node. Group C comprised metastasis-negative LPLNs in metastasis-positive patients not belonging to groups A and B (i.e. metastasis-negative LPLNs in areas other than the area with positive LPLNs). Group D comprised metastasis-negative LPLNs in metastasis-negative patients.

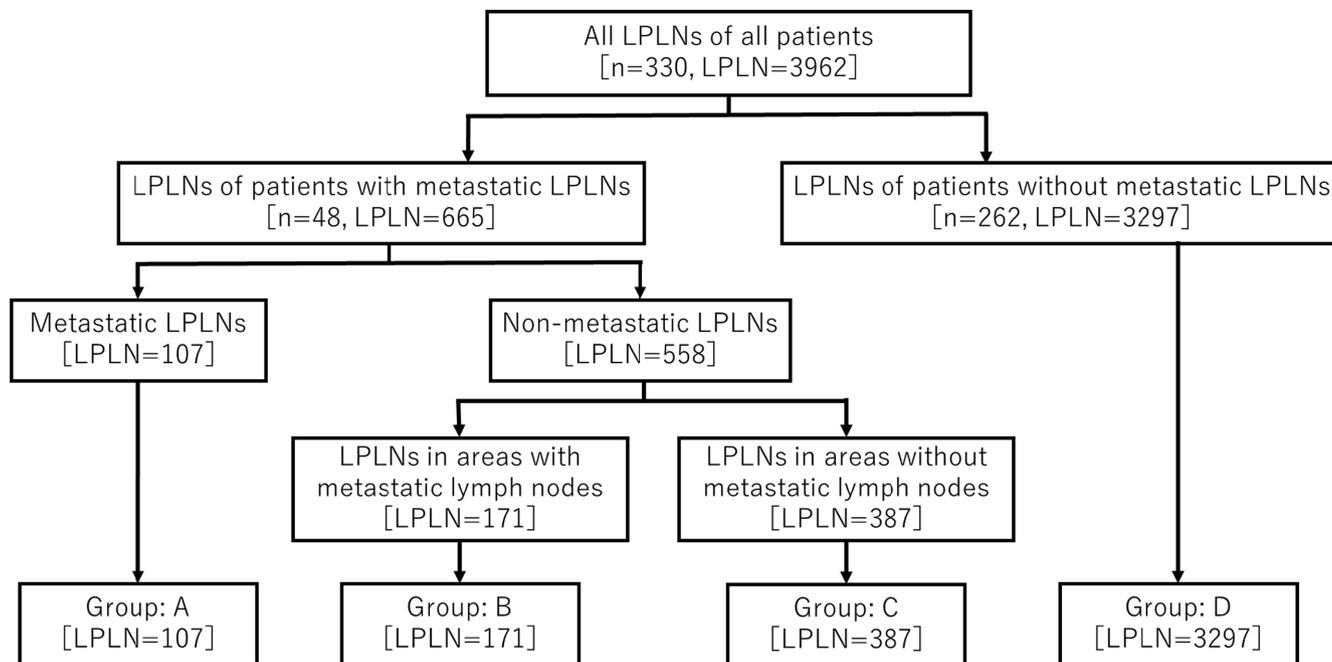


FIGURE 1 Patient and LPLN inclusion flowchart. LPLN, lateral pelvic lymph node

2.3 | Pathological measurement

The long and short axes of all LPLNs were measured on histological slides using a Vernier caliper. We first measured the maximum short axis, followed by the long axis perpendicular to it. Furthermore, the aspect ratio, calculated by dividing the short axes by the long axes, had a value between 0 and 1. A larger aspect ratio corresponded to a rounder shape, and a smaller value corresponded to a more oval or linear lymph node shape.

2.4 | Patient population with LALRC

There is a temporal evolution of treatment selection for LALRC in our institution. In the first half of the study period, NAC was mainly selected for patients with high-risk feature(s) of distant metastasis, such as multiple swollen lymph nodes in the mesorectum, and NACRT was rarely performed. All patients who underwent curative resection underwent bilateral LPLND. However, in the second half of the study period, NACRT to suppress the local recurrence rate was increasingly performed in accordance with the risk factors for local recurrences, such as cCRM and extramural vascular invasion on MRI. LPLND was not performed in low-risk patients. Approximately 58% of all patients with LALRC were selected for surgery in accordance with the first strategy, and 94% of these patients received bilateral LPLND.

2.5 | Statistical analysis

Data are expressed as median, mean, and range. The Kolmogorov-Smirnov test was used to test the normality of the data. Nonnumerical

data were analyzed using the Kruskal-Wallis test. Multiple comparisons among the four groups were adjusted using the Bonferroni correction ($P < .0083$). $P < .05$ was considered significant.

3 | RESULTS

In total, 48 patients had metastasis-positive LPLNs. The patient and tumor characteristics are presented in Tables 1 and 2, respectively. Overall, 3962 LPLNs were harvested; of these, 107, 171, 387, and 3297 LPLNs were classified into groups A (metastasis-positive LPLNs), B (metastasis-negative LPLNs in the area containing metastasis-positive LPLNs), C (metastasis-negative LPLNs in a metastasis-negative area in metastasis-positive patients), and D (metastasis-negative LPLNs in metastasis-negative patients), respectively. LPLNs of groups A, B, and C were from 48 metastasis-positive patients, and LPLNs of group D were from 262 metastasis-negative patients. Some pathological stage IV patients were included. Although these cases were in clinical stage III, they were small liver metastases or small areas of peritoneal dissemination cases found intraoperatively, and para-aortic lymph node metastasis or inguinal lymph node metastasis cases diagnosed postoperatively. All cases underwent curative resection as planned.

Table 2 shows the mean values and ranges of the long axis length, short axis length, and aspect ratio of the lymph nodes in each group. The average values (ranges) of the aspect ratio for groups A, B, C, and D are 0.68 (0.40-1.00), 0.60 (0.14-1.00), 0.49 (0.08-1.00), and 0.39 (0.05-1.00), respectively. And the aspect ratio in the (B+C+D) group of whole metastasis-negative lymph nodes was 0.42 (0.05-1.00). Figure 2 shows the group-wise distribution of the long axis length, short axis length, and aspect ratios of the lymph nodes. The mean lengths of the

TABLE 1 Patient characteristics and pathological results

	With metastatic LPLNs (%) (n = 48)	Without metastatic LPLNs (%) (n = 262)
Sex		
Male	34 (71)	183 (70)
Female	14 (29)	79 (30)
Age (years), median (range)	64 (34-83)	63(32-86)
Approach		
Open	15 (31)	86 (33)
Laparoscopy	33 (69)	176 (67)
Type of LPLND		
Bi	45 (94)	261 (99)
Right	2 (4)	1 (1)
Left	1 (2)	0 (0)
T-stage		
1	1 (2)	5 (2)
2	6 (12)	49 (19)
3	31 (65)	185 (70)
4	10 (21)	23 (9)
N-stage		
No LNM	0 (0)	165 (63)
MLNM	0 (0)	97 (37)
LPLNM	3 (6)	0 (0)
MLNM + LPLNM	45 (94)	0 (0)
M-stage		
0	40 (83)	258 (98)
1	8 (17)	4 (2)
TNM stage		
I	0 (0)	46 (17)
II	0 (0)	118 (45)
III	40 (83)	94 (36)
IV	8 (17)	4 (2)
Histopathological type		
tub1	10 (21)	62 (23)
tub2	33 (69)	177 (67)
Por/sig	2 (4)	6 (2)
Others	3 (6)	23 (8)
Lymphatic invasion		
None	9 (19)	111 (43)
Moderate	27 (56)	145 (55)
Severe	12 (25)	6 (2)
Vascular invasion		
None	3 (6)	43 (16)
Moderate	35 (73)	193 (74)
Severe	10 (21)	26 (10)

Abbreviations: LNM, lymph node metastasis; LPLN, lateral pelvic lymph node; LPLND, lateral pelvic lymph node dissection; LPLNM, lateral pelvic lymph node metastasis; MLNM, mesenteric lymph node metastasis.

TABLE 2 Lymph node morphology

Group	A (LPLN = 107)	B (LPLN = 171)	C (LPLN = 387)	D (LPLN = 3297)	B + C + D (LPLN = 3855)
Size of the LPLNs (mm)					
Long axis	8.6 (1-30)	4.7 (1-20)	4.9 (0.5-27)	4.9 (0.5-29)	4.9 (0.5-29)
Short axis	5.8 (1-18)	2.4 (0.5-13)	2.0 1.3 (0.5-10)	1.7 (0.5-14)	1.7 (0.5-14)
Aspect ratio ^a	0.68 (0.40-1.00)	0.60 (0.14-1.00)	0.49 (0.08-1.00)	0.39 (0.05-1.00)	0.42 (0.05-1.00)

Note: Values are expressed as average (range). Group A: Positive metastasis lymph node. Group B: Negative metastasis lymph node in areas with metastatic LPLNs. Group C: Negative metastasis lymph node in areas without metastatic LPLNs. Group D: Negative metastasis lymph node of patients without metastatic LPLNs. Group B + C + D: Negative metastasis lymph node.

Abbreviation: LPLN, lateral pelvic lymph node.

^aShort axis/long axis.

long and short axes in group A were significantly longer than those in the other groups ($P < .001$). Meanwhile, no significant differences in the mean lengths of the long axes were observed among groups B, C, and D. However, the short axis in group B was significantly longer than that in group D ($P < .001$); it was also longer than that in group C, but the difference was not significant ($P = .017$). The short axis was significantly longer in group C than in group D ($P < .001$). Similarly, the mean aspect ratio was significantly higher (rounder shape) in group A than in the other groups ($P < .003$). The mean aspect ratio was significantly higher in group B than in groups C and D and was significantly higher in group C than in group D ($P < .001$).

An aspect ratio cut-off of 0.4 had negative predictive value, positive predictive value, false-positive rate, and false-negative rate of 100%, 5.5%, 48%, and 0%, respectively. Meanwhile, a cut-off of 0.5

had rates of 99.8%, 7.4%, 32.6%, and 5.6%, respectively. Based on these results, the cut-off value of the aspect ratio for determining negative LPLNs was determined to be approximately 0.4. Group A did not contain any lymph nodes with an aspect ratio lower than 0.4 (oval or linear shape). The metastasis-positive LPLNs tended to be larger and more circular in shape than metastasis-negative LPLNs. Furthermore, the metastasis-negative LPLNs in the area containing metastasis-positive LPLNs (i.e. existing nearby) tended to have a larger short axis and a higher aspect ratio (roundness) than metastasis-negative LPLNs located elsewhere. Figure 3 shows a plot of the sizes of the long and short axes in each group, and a plot of the aspect ratio on the vertical axis and the size of the short axes on the horizontal axis, which allows a visual comparison of the morphology and size of the LPLNs between all groups.

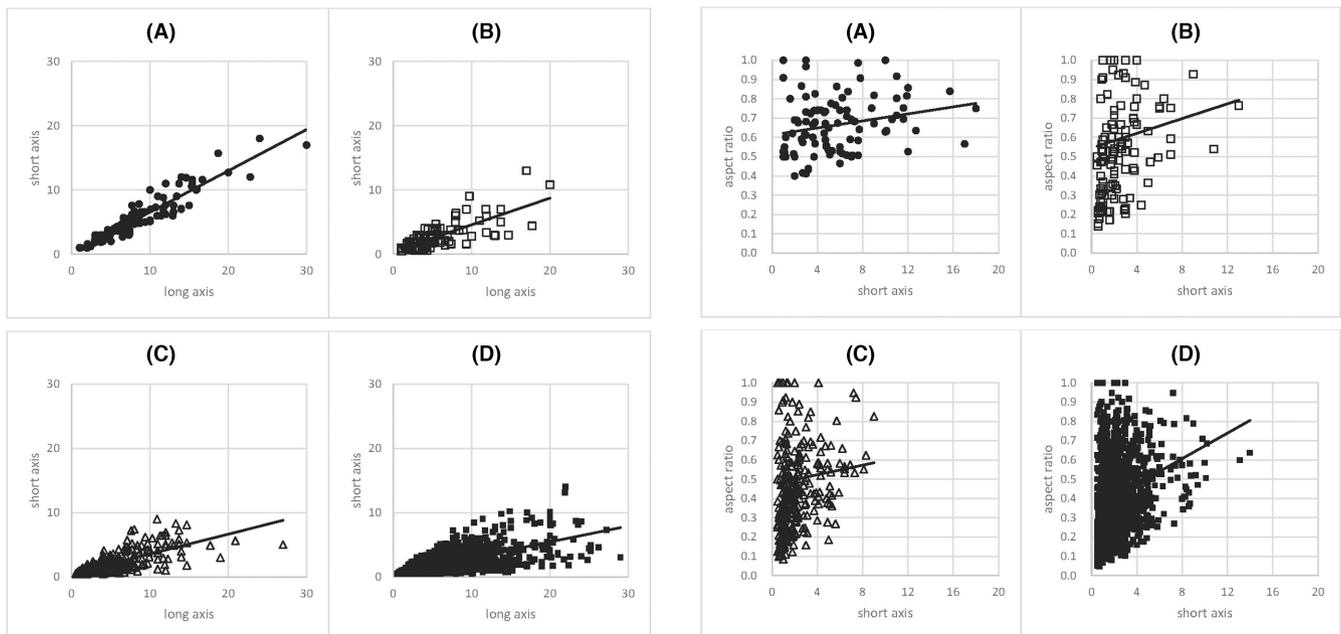


FIGURE 2 (A) Relationship between the long-axis diameter of the LPLNs and each group. (B) Relationship between the short-axis diameter of the LPLNs and each group. (C) relationships between the aspect ratios of the LPLNs and each group. LPLN, lateral pelvic lymph node; A, metastasis-positive lymph node; B, metastasis-negative lymph node in areas with metastatic LPLNs; C, metastasis-negative lymph nodes in areas without metastatic LPLNs; (D), metastasis-negative lymph nodes in patients without metastatic LPLNs

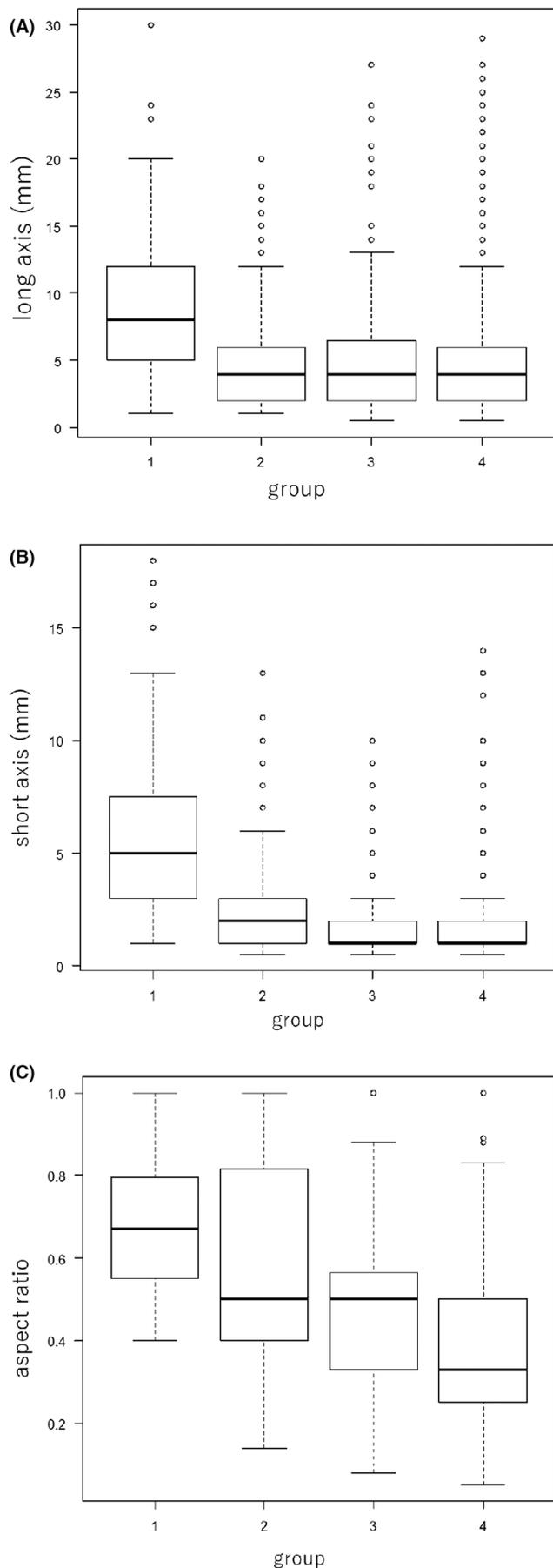


FIGURE 3 Relationship between the long and short axes diameters of the LPLNs in each group, and the relationship between the short-axis diameter and the aspect ratio of LPLN in each group. LPLN, lateral pelvic lymph node; (A), metastasis-positive lymph node; (B), metastasis-negative lymph node in areas with metastatic LPLNs; (C), metastasis-negative lymph nodes in areas without metastatic LPLNs; (D), metastasis-negative lymph nodes in patients without metastatic LPLNs

Table 3 shows the accuracy of the LPLN metastasis diagnosis when the cut-off values were 4, 7, and 10 mm for the short axis and 4, 7, and 10 mm for the long axis. When calculations were performed using the globally used 7-mm short-axis size criterion,¹⁹ the diagnostic accuracy of positive lateral metastasis was 35.6% in lymph nodes with a short axis of ≥ 7 mm. There were 76 metastasis-positive lymph nodes and 3875 lymph nodes with a short axis of < 7 mm.

Table 4 shows the accuracy of the LPLN metastasis diagnosis in each patient according to the different maximum short axes of the LPLN (11 groups, each differing by 1 mm). Figure 4 depicts the photomicrographs of typical lymph nodes from each group. The visual appearance of the metastasis-negative lymph nodes (black

TABLE 3 Accuracy of the diagnosis of metastatic LPLNs

	Size of LPLNs (mm)	Metastatic LPLNs	All LPLNs	Accuracy (%)
Short axis	≤ 0	107	3962	2.7
	≤ 4	64	361	17.7
	≤ 7	31	87	35.6
	≤ 10	19	28	67.9
Long axis	≤ 0	107	3962	2.7
	≤ 4	87	1953	4.5
	≤ 7	61	860	7.1
	≤ 10	37	412	9.0

Abbreviation: LPLN, lateral pelvic lymph node.

TABLE 4 Accuracy of metastasis diagnosis by different maximum short axes of the LPLN

Maximum LPLN short axis (mm)	Patients with metastatic LPLNs (n = 48)	All patients (n = 310)	Metastasis rate (%)
$\geq 0, < 1$	0	4	0
$\geq 1, < 2$	0	12	0
$\geq 2, < 3$	0	67	0
$\geq 3, < 4$	3	57	5.3
$\geq 4, < 5$	2	52	3.8
$\geq 5, < 6$	3	36	8.3
$\geq 6, < 7$	9	21	42.9
$\geq 7, < 8$	9	19	47.4
$\geq 8, < 9$	2	12	16.7
$\geq 9, < 10$	3	8	37.5
≥ 10	17	23	73.9

Abbreviation: LPLN, lateral pelvic lymph node.

triangles [▲]) in the areas containing metastasis-positive lymph nodes (white triangles [△]) shows that the lymph nodes in group A had a greater tendency to be round in shape than those in other groups. Metastasis-negative LPLNs were more likely to have higher aspect ratios in metastasis-positive patients (black triangles, white arrows) than in metastasis-negative patients (black triangles).

4 | DISCUSSION

Data on the aspect ratio of the lymph nodes in LALRC, which may influence local recurrence, are limited. This study found that metastasis-positive LPLNs were significantly larger and had a higher aspect ratio than did metastasis-negative LPLNs, indicating that a greater amount of metastasis occurred in larger and more circular LPLNs than in metastasis-negative LPLNs. Although small metastatic LPLNs containing cancer cells were detected, most metastasis-positive LPLNs had aspect ratios >0.5 . Moreover, all LPLNs with an aspect ratio <0.4 (oval or linear shape) were metastasis negative.

To our knowledge, there are no previous reports on the aspect ratios of LPLNs in LALRC. Most studies on the diagnosis of LPLN metastases in LALRC are primarily size-related analyses; however, some have used morphological criteria.^{11,12,20,21} Akasu et al used criteria such as an irregular border, mixed signal intensity, and the presence of a high-intensity nodule within the lymph node on MRI.²¹ Matsuoka et al reported that LPLNs with an "ovoid shape" tend to be metastasis positive, without analysis using aspect ratio criteria.^{11,12} On the other hand, similar pelvic malignancies have been reported based on the aspect ratio of pelvic lymph nodes in gynecological and bladder cancers. Nakai et al found no differences in

the MRI-measured lymph node parameters (i.e. the long axis, short axis, and aspect ratio) between gynecological cancer patients with and without metastasis.¹⁵ In contrast, in cases of bladder cancer, all elongated lymph nodes with an aspect ratio ≤ 0.4 were metastasis negative, and consistent findings were found in the present study. We measured the morphology of over 3000 LPLNs, including small lymph nodes that could not be analyzed by imaging. Moreover, to our best knowledge, this study is the first to report that lymph nodes in metastasis-positive regions have a higher aspect ratio (i.e. are closer to a rounder shape) even if they are metastasis negative. It can be surmised that lymph nodes surrounding the metastatic lymph nodes have some type of immune response similar to that of sentinel lymph nodes,^{22,23} which may also aid in diagnosing metastasis during imaging. That is, multiple rounded lymph nodes identified in the lateral pelvic region on imaging examinations may indicate a possibility that these could include metastatic lymph nodes. Conversely, lymph nodes with diameters >2 cm with a low aspect ratio may be considered as metastasis-negative.

The rate of accurate preoperative diagnosis for LPLNs has been improved using various size criteria (cut-off values); however, using the generally used criterion of a short axis ≥ 4 mm and a long axis ≥ 7 mm did not significantly improve the accuracy of diagnosis beyond 80%, despite the differences in sensitivity and specificity. When the same criteria were applied to this study, 64 of the 361 lymph nodes (17.7%) with a short axis ≥ 4 mm were metastasis-positive, and 43 of the 3601 lymph nodes (1.2%) with a short axis <4 mm were metastasis-positive. However, as seen in Table 4, of the 140 cases with a maximum minor axis <4 mm, 3 (2.1%) were metastasis-positive cases. In total, three out of 310 cases (0.9%) were metastasis-positive. Furthermore, among the 61 lymph nodes with a

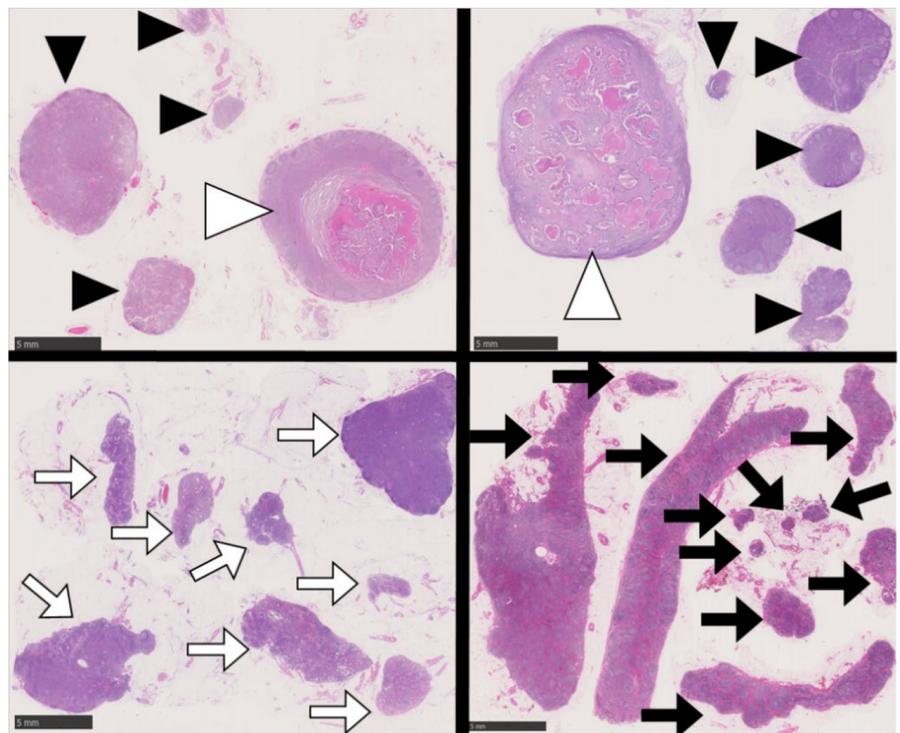


FIGURE 4 LPLNs in each group. White arrowhead: Group A; black arrowhead: Group B; white arrow: Group C; black arrow: Group D. LPLN, lateral pelvic lymph node; A, metastasis-positive lymph node; B, metastasis-negative lymph node in areas with metastatic LPLNs; C, metastasis-negative lymph nodes in areas without metastatic LPLNs; D, metastasis-negative lymph nodes in patients without metastatic LPLNs

long axis ≥ 7 mm, 7.1% were metastasis-positive; meanwhile, among the lymph nodes with a long axis < 7 mm, 46 (1.5%) were metastasis-positive. Therefore, the rate of accurate diagnosis according to size was 17.7% for a cut-off value of 4 mm for the short axis and 7.1% for a cut-off value of 7 mm for the long axis. Meanwhile, combining the size and aspect ratio of the lymph nodes improved the negative predictive value to almost 100%.

In the current study, we used clinical and pathological data from patients not treated by NACRT. The reasons for exclusion are as follows: (a) In NACRT cases, metastasis-positive LPLNs often disappear, and the size and aspect ratio change at that time. (b) This study aimed to investigate the potential of the size and aspect ratio of metastatic and non-metastatic LPLNs as low-risk markers for LALRC without treatment by NACRT or LPLND. However, in the next step, similar studies are needed for the positive and negative LPLNs (metastasis-negative nodes include both initially-metastasis-negative and cancer-disappeared nodes) in NACRT treated patients.

The present study has the following limitations. First, we included only the surgery-first cases that did not receive any preoperative therapy. Therefore, the findings on diagnostic accuracy with respect to the presence or absence of metastasis were not affected by preoperative treatment. Consequently, the extent to which cancerous tissue is eliminated by chemoradiotherapy is unknown. Given that the analysis did not include a preoperative treatment group, some high-risk patients were excluded from the analysis because of changes in the indications for preoperative treatment over time. Second, LPLNs were categorized according to their largest diameter. However, this maximum secant plane does not necessarily coincide with the axial plane, which is commonly used for MRI diagnosis. When the slides were prepared, the lymph nodes were compressed for fixation, resulting in some changes in size. Third, we did not include small LPLNs that would not be recognized on MRI, given that a thorough identification of the lymph nodes is performed by the surgeon in charge of the surgery before formalin fixation of the excised fatty tissue. Lastly, this was a single-center, retrospective study.

5 | CONCLUSIONS

Metastatic LPLNs in LALRC are significantly larger and rounder in shape. All lymph nodes with an aspect ratio < 0.4 were metastasis-negative. These findings may be important for determining the indications for LPLND in rectal cancer.

ACKNOWLEDGEMENTS

The authors would like to thank M. Narikiyo for technical assistance with the experiments.

DATA AVAILABILITY STATEMENT

The data and methods used in the analysis can be obtained from the corresponding author upon reasonable request.

DISCLOSURE

Conflict of Interest: Authors declare no conflicts of interest for this article.

Author Contributions: All authors declare that they have contributed to this article and have approved the final submitted version. YS and TS collected the data, wrote the manuscript, and contributed equally to the manuscript.

Ethical Approval and Consent to Participate: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution, and it conforms to the provisions of the Declaration of Helsinki. Committee of National Cancer Center Hospital, Approval No. 2018-100. Informed consent was obtained from all the subject(s) and/or guardian(s).

ORCID

Yushi Suzuki  <https://orcid.org/0000-0002-0388-9269>

Masaaki Ito  <https://orcid.org/0000-0002-1101-2707>

REFERENCES

1. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery—the clue to pelvic recurrence? *Br J Surg.* 1982;69(10):613–6.
2. Ogura A, Konishi T, Cunningham C, Garcia-Aguilar J, Iversen H, Toda S, et al. Neoadjuvant (chemo)radiotherapy with total mesorectal excision only is not sufficient to prevent lateral local recurrence in enlarged nodes: results of the multicenter lateral node study of patients with low cT3/4 rectal cancer. *J Clin Oncol.* 2019;37(1):33–43.
3. Kim TG, Park W, Choi DH, Park HC, Kim SH, Cho YB, et al. Factors associated with lateral pelvic recurrence after curative resection following neoadjuvant chemoradiotherapy in rectal cancer patients. *Int J Color Dis.* 2014;29(2):193–200.
4. Bosset JF, Collette L, Calais G, Mineur L, Maingon P, Radosevic-Jelic L, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. *N Engl J Med.* 2006;355(11):1114–23.
5. Fujita S, Mizusawa J, Kanemitsu Y, Ito M, Kinugasa Y, Komori K, et al. Mesorectal excision with or without lateral lymph node dissection for clinical stage II/III lower rectal cancer (JCOG0212): a multicenter, randomized controlled, noninferiority trial. *Ann Surg.* 2017;266(2):201–7.
6. Kroon HM, Malakorn S, Dudi-Venkata NN, Bedrikovetski S, Liu J, Kenyon-Smith T, et al. Local recurrences in western low rectal cancer patients treated with or without lateral lymph node dissection after neoadjuvant (chemo)radiotherapy: an international multi-Centre comparative study. *Eur J Surg Oncol.* 2021;47(9):2441–9.
7. Ogura A, Konishi T, Beets GL, Cunningham C, Garcia-Aguilar J, Iversen H, et al. Lateral nodal features on restaging magnetic resonance imaging associated with lateral local recurrence in low rectal cancer after neoadjuvant chemoradiotherapy or radiotherapy. *JAMA Surg.* 2019;154(9):e192172.
8. Ogawa S, Hida J, Ike H, Kinugasa T, Ota M, Shinto E, et al. Selection of lymph node-positive cases based on perirectal and lateral pelvic lymph nodes using magnetic resonance imaging: study of the Japanese society for cancer of the colon and rectum. *Ann Surg Oncol.* 2016;23(4):1187–94.
9. Kobayashi H, Kikuchi A, Okazaki S, Ishiguro M, Ishikawa T, Iida S, et al. Diagnostic performance of multidetector row computed tomography for assessment of lymph node metastasis in patients with distal rectal cancer. *Ann Surg Oncol.* 2015;22(1):203–8.
10. Ishihara S, Kawai K, Tanaka T, Kiyomatsu T, Hata K, Nozawa H, et al. Diagnostic value of FDG-PET/CT for lateral pelvic lymph node

- metastasis in rectal cancer treated with preoperative chemoradiotherapy. *Tech Coloproctol.* 2018;22(5):347–54.
11. Matsuoka H, Masaki T, Sugiyama M, Atomi Y, Ohkura Y, Sakamoto A. Morphological characteristics of lateral pelvic lymph nodes in rectal carcinoma. *Langenbeck's Arch Surg.* 2007;392(5):543–7.
 12. Matsuoka H, Nakamura A, Masaki T, Sugiyama M, Nitatori T, Ohkura Y, et al. Optimal diagnostic criteria for lateral pelvic lymph node metastasis in rectal carcinoma. *Anticancer Res.* 2007;27(5B):3529–33.
 13. Noji T, Kondo S, Hirano S, Tanaka E, Suzuki O, Shichinohe T. Computed tomography evaluation of regional lymph node metastases in patients with biliary cancer. *Br J Surg.* 2008;95(1):92–6.
 14. Tohnosu N, Onoda S, Isono K. Ultrasonographic evaluation of cervical lymph node metastases in esophageal cancer with special reference to the relationship between the short to long axis ratio (S/L) and the cancer content. *J Clin Ultrasound.* 1989;17(2):101–6.
 15. Nakai G, Matsuki M, Inada Y, Tatsugami F, Tanikake M, Narabayashi I, et al. Detection and evaluation of pelvic lymph nodes in patients with gynecologic malignancies using body diffusion-weighted magnetic resonance imaging. *J Comput Assist Tomogr.* 2008;32(5):764–8.
 16. Li Y, Diao F, Shi S, Li K, Zhu W, Wu S, et al. Computed tomography and magnetic resonance imaging evaluation of pelvic lymph node metastasis in bladder cancer. *Chin J Cancer.* 2018;37(1):3.
 17. Fujita S, Akasu T, Mizusawa J, Saito N, Kinugasa Y, Kanemitsu Y, et al. 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. *Lancet Oncol.* 2012;13(6):616–21.
 18. Hashiguchi Y, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T, et al. Japanese Society for Cancer of the colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. *Int J Clin Oncol.* 2020;25(1):1–42.
 19. Lee D, Matsuda T, Yamashita K, et al. Significance of lateral pelvic lymph node size in predicting metastasis and prognosis in rectal cancer. *Anticancer Res.* 2019;39(2):993–8.
 20. Ogawa S, Itabashi M, Inoue Y, Ohki T, Bamba Y, Koshino K, et al. Lateral pelvic lymph nodes for rectal cancer: a review of diagnosis and management. *World J Gastrointest Oncol.* 2021;13(10):1412–24.
 21. Akasu T, Iinuma G, Takawa M, Yamamoto S, Muramatsu Y, Moriyama N. Accuracy of high-resolution magnetic resonance imaging in preoperative staging of rectal cancer. *Ann Surg Oncol.* 2009;16(10):2787–94.
 22. Murphy J, Pocard M, Jass JR, O'Sullivan GC, Lee G, Talbot IC. Number and size of lymph nodes recovered from dukes' B rectal cancers: correlation with prognosis and histologic antitumor immune response. *Dis Colon Rectum.* 2007;50(10):1526–34.
 23. Pihl E, Nairn RC, Milne BJ, Cuthbertson AM, Hughes ES, Rollo A. Lymphoid hyperplasia: a major prognostic feature in 519 cases of colorectal carcinoma. *Am J Pathol.* 1980;100(2):469–80.

How to cite this article: Suzuki Y, Sasaki T, Hasegawa H, Ikeda K, Teramura K, Tsukada Y, Morphological characteristics of lateral pelvic lymph nodes in locally advanced lower rectal cancer: A retrospective study. *Ann Gastroenterol Surg.* 2022;6:795–803. <https://doi.org/10.1002/ags3.12590>