

Original Research Article

## Pre-operative Evaluation of Lateral Pelvic Lymph Node Metastasis in Lower Rectal Cancer: Comparison of Three Different Imaging Modalities

Kunihiko Amano<sup>1)</sup>, Minoru Fukuchi<sup>1)</sup>, Kensuke Kumamoto<sup>2)</sup>, Satoshi Hatano<sup>1)</sup>, Hitoshi Ohno<sup>3)</sup>, Hisato Osada<sup>3)</sup>, Keiichiro Ishibashi<sup>1)</sup> and Hideyuki Ishida<sup>1)</sup>

1) *Department of Digestive Tract and General Surgery, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan*

2) *Department of Gastroenterological Surgery, Kagawa University, Kagawa, Japan*

3) *Department of Radiology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan*

### Abstract

**Objectives:** The pre-operative diagnostic value of detecting lateral pelvic lymph node (LPLN) metastasis with magnetic resonance imaging, multidirectory computed tomography, and positron emission tomography/computed tomography was investigated in lower rectal cancer patients.

**Methods:** We retrospectively evaluated, using the three different modalities, the metastatic status of LPLNs in four regions, including both the internal iliac and the obturator, in 46 patients affected by lower rectal cancer patients who underwent LPLN dissection. The size inclusion criterion for LPLN metastasis was set at 6 mm in the short axis diameter. Histological examination was performed for determining the false positive and negative rate of LPLNs metastasis detection.

**Results:** Among 184 LPLNs regions, 17 (9%) were positive for metastasis. The region-based sensitivity, specificity, and accuracy rate did not differ among the three tested diagnostic modalities. Moreover, a significant increase in these rates could not be observed when the modalities were combined. Of 184 regions, 8 (4.4%) were false negative, whereas 2 (1.1%) were false positive. The histological pattern of metastatic regions did not differ in 8 false negative LPLNs.

**Conclusions:** Each modality had a similar detection power for LPLNs metastasis, with a cut-off value at 6 mm in the short axis diameter. However, the sensitivity of all the modalities was slightly low, along with the number of false negative LPLNs. Further reduction of the false negative rate with these modalities may be difficult because of an inherent limitation of current imaging technologies to accurately detect lymph node metastases.

### Keywords

lower rectal cancer, lateral pelvic lymph node metastasis, computed tomography, magnetic resonance imaging, positron emission tomography

J Anus Rectum Colon 2020; 4(1): 34-40

### Introduction

Mesorectal excision (ME), which included total mesorectal excision (TME) or tumor-specific ME, has become the

standard surgical procedure for treating lower rectal cancer (LRC). However, the treatment strategy for treating lateral pelvic lymph node (LPLN) metastasis differs between Japan and Western countries. In Japan, ME with LPLN dissection

is the standard surgical procedure for treating patients with advanced LRC, as the frequency of LPLN metastasis has been reported to be approximately 20%[1]. In a recent phase III study (JCOG0212), ME with LPLN dissection showed a significantly lower local recurrence rate, especially in the lateral pelvis, when compared with ME alone in LRC patients with stage II or III[2]. In Western countries, pre-operative chemoradiotherapy is a standard therapy for LRC. LPLN dissection is not usually performed, as LPLN metastasis is considered to be a systemic disease, and LPLN dissection may cause significant post-operative genitourinary complications[3]. Thus, when the presence of an LPLN metastasis in advanced LRC patients is suspected, a combined treatment strategy is employed to improve clinical outcomes[4]. Therefore, an accurate pre-operative diagnosis of LPLN metastasis is required to select LRC patients for LPLN dissection.

Lymph node metastasis of LRC is usually evaluated using different imaging modalities, such as multiple detector (MD) computed tomography (CT), and magnetic resonance imaging (MRI)[5]. MRI has a superior contrast resolution in soft tissue and is generally used for evaluating the nodal stage of rectal cancer. In a recent meta-analysis, the sensitivity and specificity of MRI for the lymph node metastasis diagnosis were reported to be 77% and 71%, respectively[6], but this study only examined the perirectal (mesorectal) lymph nodes. Several studies from Japan reported the diagnostic value of MRI for the detection of LPLN metastasis in LRC without pre-operative therapy[7-11]. According to these studies, the sensitivity and specificity of MRI for the detection of LPLN metastasis were ranging between 43.8%-87% and 79.7%-98.5%, respectively. The range of sensitivity thus appears to be highly variable and relatively low. Radiographic conditions and diagnostic size criteria may affect the detectability of LPLN metastasis.

The size criteria for LPLN metastasis detection has not been fully examined for MRI and CT imaging. Previous studies reported that the cut-off value of LPLN metastasis ranged between 4 and 10 mm[7-11]. In the JCOG0212 trial, lymph nodes with a short-axis diameter of <10 mm as seen by CT or MRI imaging were defined as negative for detecting LPLN metastasis[2]. We previously investigated the shrinkage ratio between resected LPLN specimens and paraffin-embedded sections in metastatic and non-metastatic LPLNs and reported that short axis diameter of 5.4 mm might be the optimal cut-off for predicting LPLN metastasis in the living body[12]. Therefore, the evaluation of LPLN metastasis in imaging studies is necessary to determine the optimal treatment strategy for patients with advanced LRC.

The utility of <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) for lymph node staging evaluation of colorectal cancer has already been reported[13]. This recent meta-analysis demonstrated

that the pooled estimates of sensitivity and specificity of PET/CT in the detection of pre-operative lymph node involvement in colorectal cancer patients were 42.9% and 87.9%, respectively[13]. These values are similar to those of MRI and CT. To our knowledge, the diagnosis of LPLN metastasis on LRC patients with the combination of MRI, (MD) CT, and PET/CT has not been investigated yet.

In this study, we pre-operatively evaluated the region-based diagnostic values of the three imaging modalities for detecting LPLN metastasis in LRC patients who underwent ME and LPLN dissection without pre-operative chemoradiation, to assess the optimal pre-operative diagnosis strategy, based on criteria established in our previous studies[12,14].

## Methods

### Patients

We retrospectively assessed 46 LRC patients who underwent pre-operative MRI, MDCT, and PET/CT imaging followed by surgical ME and LPLN dissection without pre-operative chemoradiation. We routinely performed bilateral LLN dissection with TME for surgically low-risk patients with locally advanced LRC (localized below the peritoneal reflection), while we avoided standard LLN dissection but performed sampling of LLNs with TME for elderly patients (in principle, over 75 years old) and/or those with co-morbid diseases, such as cases with American Society of Anesthesiologists' (ASA) physical status ( $\geq 3$ ). The patients enrolled in the study were hospitalized at the Saitama Medical Center of the Saitama Medical University between October 1997 and October 2016. All the patients underwent LPLN dissection in four different regions, including both the internal iliac and the obturator region. The external iliac and middle sacral regions, which were dissected in some patients as well, were excluded from this study. A total of 184 LPLNs regions from 46 LRC patients were analyzed in this study. The pathological diagnosis was performed according to the Japanese Classification of Colorectal Carcinoma guidelines[15]. The characteristics of 46 patients with LRC are presented in Table 1. There were 25 male and 21 female patients with a median age of 65 years (range: 35-78 years). Pathologically, LPLN metastases were identified in 12 patients (26%) and in 17 regions (9%) out of the 184 total regions. Consequently, of the 46 patients who underwent TME and LPLN dissection, 31 were subjected to a low anterior resection, 2 to an intersphincteric resection, and 13 to an abdominoperineal resection.

The study was approved by the Local Ethics Committee of the Saitama Medical Center of the Saitama Medical University (No. 833-II and 2073). Written informed consent for participation in the clinical trial was obtained from each participating patient.

**Table 1.** Clinicopathological Characteristics of 46 Patients with Lower Rectal Cancer.

Characteristic	
Median age (range), years	65 (35-78)
Gender	
Male/female	25/21
Median tumor size (range), mm	48 (16-105)
Histological type	
Well/Moderately/Poorly differentiated/Mucinous	10/33/1/2
Pathological tumor depth	
T1/2/3/4	1/10/34/1
Pathological PRLN	
Negative/positive	24/22
Pathological LPLN (regions)	
Negative/positive	34/12 (17)
Pathological stage	
I/ II/ IIIa/ IIIb/ IV	9/11/5/20/1
Lymphatic invasion	
L0/1	10/36
Venous invasion	
V0/1	5/41
Surgical procedure	
(Ultra) low anterior resection	31
Intersphincteric resection	2
Abdominoperineal resection	13

RPLN, perirectal lymph node; LPLN, lateral pelvic lymph node.

### Study 1

We have previously compared non-metastatic LPLN in the living body and paraffin-embedded LPLN metastatic sections to determine the optimal size of metastatic LPLN. We reported that the optimal short axis cut-off value for determining the metastasis status in LPLN was  $\geq 6$  mm in the living body [12,14]. Based on our previous results, in this study, LPLNs larger than 6 mm in their short axis diameter in the MRI and MDCT images were diagnosed as positive of metastasis. For PET/CT scans, an abnormal increase in the  $^{18}\text{F}$ -FDG uptake was the positive criterion for metastasis detection.

MRI was performed using a 1.5 system (Siemens, Magnetom Avanto 1.5T, Japan). Sequences obtained were T1-weighted (TR: 350 ms, TE: 12 ms) and T2-weighted images (TR: 3620 ms, TE: 86 ms). The matrix size was  $512 \times 512$  mm, the slice thickness was 5 mm, and the inter-slice gap was 1.5 mm. Either gadodiamide or gadobutrol was used as the contrast agent. CT scans were performed using a Siemens Definition Flash Emotion 16 System with 128 parallel detector rows (Siemens, Japan) from 2008. The slice thickness was 1 mm using this system. Before the use of that system, the slice thickness of CT was 5 mm. Nonionic intravenous contrast material was administered. PET/CT scans were acquired on a Siemens Biograph 16 PET/CT system at

least 1 h after intravenous injection of  $^{18}\text{F}$ -FDG.

The first author independently evaluated these findings under the supervision by two experienced radiologists without the acknowledgment of the LPLN metastatic status by pathological diagnosis until a consensus in the pre-operative status had been reached. The data was prospectively collected and recorded and retrospectively analyzed.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rates were calculated based on the region comparison of the imaging diagnoses with the pathological diagnosis.

### Study 2

We examined the pathological characteristics of each LPLNs in discrepancy cases between the preoperative diagnosis and the pathological diagnosis. Metastasis negative was pre-operatively diagnosed using more than two image modalities, but those that were metastatic positive in the histological diagnosis were regarded as false negatives. On the contrary, metastasis positive was pre-operatively diagnosed using more than two image modalities, but metastasis negative was histologically determined as false positive. The short and long axis diameter of the LPLN on paraffin-embedded sections was measured. Regarding the false-negative LPLNs, the distribution pattern of cancer cells was categorized into three types: focal type, diffuse type, and intermediate type. In addition, the occupation area of cancer cells on the maximum diameter section was calculated using the image-J software (Version 1.51, NIH, USA). Regarding the area ratio, the ratio of the cancer spread in the lymph node's maximum diameter was divided into three stages: less than 30%, 30% to 69%, and 70% or more.

### Statistical analysis

Statistical evaluation was performed using the  $\chi^2$  test and Fisher's exact probability test. All statistical analyses were performed with JMP 5.0 software (SAS Institute, Cary, NC, USA), and  $p$  values  $< 0.05$  were considered statistically significant.

## Results

### Diagnostic values of MRI, MDCT, and PET/CT for LPLN metastasis

The results obtained from MRI, MDCT, and PET/CT imaging were compared with the pathological results of specimens (Table 2). The overall region-based sensitivity was complete, the same at 35.3% in each modality. When diagnosed by at least one positive finding among MRI, CT, or PET/CT (combination diagnosis), the value of sensitivity was 41.7%. The specificity and accuracy were almost the same in each modality (Table 2).

**Histological examinations for LPLNs showing false positive and false negative results**

Of the 46 patients and 184 regions analyzed in this study, we found 9 cases and 10 regions with a discrepancy in the

pre-operative imaging diagnosis and the pathological diagnosis; we also found seven and eight false negative cases and regions and two and two false positive cases and regions, respectively (Table 3).

Of the eight false positive regions, seven were determined to be negative by all the modalities. The LPLN short axis diameter in paraffin-embedded sections in these cases ranged from 4 to 7 mm, though the size determined by MDCT or MRI was less than 4 mm. The pattern of the metastatic region was focal type in two LPLNs, diffuse type in five LPLNs, and intermediate type in one LPLN (Table 3 and Supplementary Figure 1). Regarding the area ratio, the occupation cancer cell rate was over 70% in six LPLNs.

Two false positive regions were diagnosed using MRI and PET/CT (Table 3). The LPLNs short axis diameter of paraffin-embedded sections was 5 and 10 mm, respectively, leading to an estimated size of more than 6 mm, which was above the cut-off value for all the imaging modalities. In the histological examinations of these LPLNs, no inflammatory changes were observed.

**Discussion**

It is important to accurately identify LRC patients with LPLN metastasis to determine the optimal treatment strategy for locally advanced LRC. The clinical size criteria of LPLN metastasis detected with imaging multimodalities have not been established yet. We previously investigated the size criteria of LPLNs using dissected LPLNs and paraffin-embedded specimens and reported that a short axis diameter of 5-6 mm should be used as a cut-off value for predicting the presence of LPLN metastasis[12]. In this study, we validated this cut-off value for an accurate pre-operative diagnosis using MRI and MDCT[12]. Furthermore, we analyzed the detectability of LPLN metastasis with PET/CT. In our

**Table 2.** Diagnostic Performance of MRI, CT and PET/CT for Lateral Pelvic Lymph Node Metastasis on a Per-region Basis.

MRI diagnosis		Histological diagnosis		
		Positive	Negative	
Positive		6	5	
Negative		11	162	
Sensitivity	Specificity	PPV	NPV	Accuracy
35.3%	97.0%	54.6%	94.0%	91.3%

  

CT diagnosis		Histological diagnosis		
		Positive	Negative	
Positive		6	0	
Negative		11	167	
Sensitivity	Specificity	PPV	NPV	Accuracy
35.3%	100%	100%	96.7%	94.0%

  

PET/CT diagnosis		Histological diagnosis		
		Positive	Negative	
Positive		6	3	
Negative		11	164	
Sensitivity	Specificity	PPV	NPV	Accuracy
35.3%	98.2%	66.7%	95.1%	92.4%

  

Combination diagnosis of MRI, CT or PET/CT		Histological diagnosis		
		Positive	Negative	
Positive		5	0	
Negative		7	172	
Sensitivity	Specificity	PPV	NPV	Accuracy
41.7%	100%	100%	97.3%	96.2%

PPV, positive predictive value; NPV, negative predictive value.

**Table 3.** The Diagnostic Discrepancy Cases of Lateral Pelvic Lymph Node Regions.

	Age	Sex	Histological type	Pathological positive	CT (short axis)	MRI (short axis)	PET/CT	Actual size of LN	Metastatic pattern	Occupation rate	
False negative	1	67	M	tub2	R-IIN	6mm	n.d.	negative	5x5mm	focal	<30%
	2	66	M	tub2>tub1	L-ON	4mm	4mm	negative	5x4mm	diffuse	70%<
	3	67	M	tub2>tub1	L-IIN	n.d.	3mm	negative	8x7mm	diffuse	70%<
	4	72	F	tub2>tub1	R-ON	3mm	3mm	negative	10x8mm	intermediate	70%<
	5	46	M	muc, tub1	R-IIN	3mm	4mm	negative	7x5mm	diffuse	70%<
	6	46	M	muc, tub1	L-ON	3mm	2mm	negative	4x4mm	diffuse	70%<
	7	54	M	tub2>muc	R-IIN	3mm	3mm	negative	4x4mm	diffuse	70%<
	8	76	F	tub2>tub1	L-IIN	n.d.	2mm	negative	6x5mm	focal	30%~70%
False positive	1	63	M	tub1>tub2	-	-	L-IIN 7mm	L-IIN positive	7x5mm	-	-
	2	60	F	tub2>tub1	-	-	R-ON 12mm	R-ON positive	15x10mm	-	-

R=Right, L=Left, IIN=Internal Iliac Nodes, ON=Obturator Nodes

**Table 4.** Studies of MRI, CT Preoperative Diagnosis and Criteria for Lateral Pelvic Lymph Node Metastasis.

Study	n	Modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Size criteria	Morphologic criteria	Year
Arii et al	55	MRI	56	97	91	81	83	7mm	round shape	2006
		CT	33	78	8	95	75	7mm	round shape	
Matsuoka et al	51	MRI	67	83			78	5mm short axis	ovoid shape	2007
Akasu et al	104	MRI	87	87	52	97	87	4mm short axis		2007
Ishibe et al	84	MRI	43.8	98.5	87.5	88.1	88.1	10mm		2016
Ogawa et al	268	MRI	68.6	79.7	44.3	91.5	77.6	5mm		2016
	280 (left)	MRI	70.8	81	43.6	93.1	79.3	short axis		

PPV, positive predictive value; NPV, negative predictive value.

cohort, the sensitivity of MRI, MDCT, and PET/CT was 35.3%, whereas the specificity was 97.0%, 100%, and 98.2%, respectively. Moreover, the accuracy of the three modalities was 91.3%, 94%, and 92.4%, respectively. Thus, we obtained similar results in all the modalities tested. When these modalities were combined for pre-operative diagnosis, we observed no significant changes. Therefore, we concluded that each modality alone could be useful to predict LPLN metastasis and that a combination strategy does not increase the diagnostic power.

A recent meta-analysis reported that the sensitivity and specificity of MRI for diagnosis of pararectal and/or mesenteric lymph node metastasis of rectal cancer were 77% and 71%, respectively[6]. Regarding the pre-operative diagnosis of LPLN metastasis ability, five Japanese imaging studies using MRI and/or (MD) CT have been published (Table 4)[7-11]. The studies using MRI showed that the sensitivity, specificity, PPV, NPV, and accuracy were in the range of 43.8%-87%, 79.7%-98.5%, 43.6%-91%, 81%-97%, and 77.6%-88.1%, respectively, using a size criteria ranging from 4 to 10 mm at the short axis. Our MRI results were similar to those reported in these reports. Arii et al.[7] reported that the accuracy of MRI in detecting the LPLN metastasis was significantly higher than CT (83% vs. 77%, respectively) because of the different slice thickness (10 mm CT vs. 7 mm MRI). We found no significant difference between MRI and CT, probably because the slice thickness condition was the same.

PET/CT is also used to detect lymph node metastasis of colorectal cancer. In a recent meta-analysis, the sensitivity and specificity of PET/CT for the diagnosis of lymph node metastasis of colorectal cancer were 42.9% and 87.9%, respectively[13]. Moreover, there is no conclusive evidence to support the routine clinical application of PET/CT to determine the nodal staging. However, PET/CT could be used to strengthen the diagnosis of a suspected lymph node metastasis detected by other imaging modalities. In the present

study, we found that the sensitivity and specificity of PET/CT for the diagnosis of LPLNs were 35.3% and 98.2%, respectively, indicating results consistent with the meta-analysis[13]. To our knowledge, the diagnostic values of PET/CT for LPLNs metastasis were evaluated for the first time in this study. MRI, CT, and PET/CT are complementary imaging modalities for the nodal staging of LPLN, and each offers its own strength and weakness. Consequently, the diagnostic values of these modalities may require a further evaluation based not only on the size criterion but also on other criteria, such as FDG accumulation. However, MRI is currently accepted as the standard available modality for the nodal staging of LPLN.

It is well established that the nodal size has a limited value for assessing the presence of lymph node metastasis. A recent study (JCOG0212) showed that LPLNs with a short axis less than 10 mm, detected MRI or CT, were pre-operatively classified as negative nodes[2]. Previous reports[16,17] showed that the most frequently used size criteria for distinguishing positive from negative nodes in rectal cancer (5 mm cut-off) have a sensitivity of 68% and a specificity of 78%. In these reports, the cut-off setting of the size criteria varied, and in most cases, the setting basis was unclear. Brown et al.[16] have reported that the cut-off for determining the status of a node was approximately 6 mm for mesorectum lymph nodes observed with MRI, as the size of malignancy nodes was  $\geq 7$  mm. We previously reported that the sensitivity of detecting metastatic mesorectum lymph nodes was 90% when the cut-off value of the short axis diameter was set at 6.2 mm[14]. In that study, we confirmed that a short axis size of approximately 5 mm was sufficient to detect LPLN metastasis[14]. Thus, according to different studies, including ours[12,14], the 6 mm cut-off value might be reasonable for evaluating of LPLN metastasis.

In this study, the sensitivity for detecting LPLN metastasis was still relatively low for any modalities. Moreover, we found eight false negative regions. Out of the eight false

negative regions, the actual short axis size was smaller than 6 mm in six false negative LPLNs. Interestingly, these LPLNs were not detected by PET/CT. Therefore, it might be impossible to detect LPLN metastasis using a size criterion for smaller than 5 mm. Although the actual LPLNs size was large in two false negative LPLNs, their short axis diameter as determined by MRI and MDCT was estimated to be smaller. Regarding CT and MRI, the size of the preoperative lymph node metastasis may not be evaluated correctly, depending on the diameter of the sliced part. A previous report demonstrated that the nodal margins and the internal nodal characteristics are the most reliable indicators of the presence of a lymph node metastasis[16]. No significant tendency was found in the type and rate of lymph node metastasis. Our results suggest that the pattern of metastatic regions and cancer cells' occupation rate are not associated with improvement in the detection of LPLN metastasis. We speculate that the frequency of false negative cases is not zero because of the limits of diagnostic imaging modalities.

One of the limitation of this study may be the 5 mm slice thickness in both of CT and MRI. Recently, MRI with 3 mm slice thickness and MDCT with 1 mm slice thickness are available in clinical practice. We used MDCT with a 1 mm slice thickness from 2008. As mentioned above, the actual LPLNs size of short axis diameter was large in only two of eight false negative LPLNs. Although high-resolution images would be improved in these modalities, we need to find out if the detection ability of metastatic LPLNs in patients with LRC increases in the future course.

In the present study, we showed that MRI, MDCT, and PET/CT have the same degree of detection ability of metastatic LPLNs in patients with LRC, using a short axis diameter cut-off of 6 mm. We confirmed that might be useful to identify LRC patients with LPLN metastasis using these imaging modalities to determine the optimal treatment strategies. However, a further reduction of false negative cases will be required using current imaging technology to detect lymph node metastases accurately.

#### Conflicts of Interest

There are no conflicts of interest.

#### Author Contributions

Kunihiko Amano, Minoru Fukuchi, and Kensuke Kumamoto drafted the manuscript. Kunihiko Amano, Minoru Fukuchi, Kensuke Kumamoto, Satoshi Hatano, Keiichiro Ishibashi, and Hideyuki Ishida performed clinical management of these patients. Kunihiko Amano, Hisato Osada, and Hitoshi Ohno analyzed lateral lymph node metastasis in imaging modalities. Keiichiro Ishibashi and Hideyuki Ishida conceived and designed the study and edited the manuscript. All authors read and approved the final manuscript.

#### Approval by Institutional Review Board (IRB)

This research was approved by the Institutional Review Board at Saitama Medical Center, Saitama Medical University (No. 833-II and 2073), and the Ethics Committee at Saitama Medical University and was conducted according to the guidelines put forth in the Declaration of Helsinki.

#### References

1. Watanabe T, Muro K, Ajioka Y, et al. Japanese Society for Cancer of the Colon and Rectum: Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines. 2016 for the treatment of colorectal cancer. *Int J Clin Oncol*. 2018 Feb; 23(1): 1-34.
2. Fujita S, Mizusawa J, Kanemitsu Y, 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 Aug; 266(2): 201-7.
3. van Gijn W, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. *Lancet Oncol*. 2011 Jun; 12(6): 575-82.
4. Akiyoshi T, Matsueda K, Hiratsuka M, et al. Indications for lateral pelvic lymph node dissection based on magnetic resonance imaging before and after preoperative chemoradiotherapy in patients with advanced low-rectal cancer. *Ann Surg Oncol*. 2015 Dec; 22(3): S614-20.
5. Kijima S, Sasaki T, Nagata K, et al. Preoperative evaluation of colorectal cancer using CT colonography, MRI, and PET/CT. *World J Gastroenterol*. 2014 Dec; 20(45): 16964-75.
6. Al-Sukhni E, Milot L, Fruitman M, et al. Diagnostic accuracy of MRI for assessment of T category, lymph node metastases, and circumferential resection margin involvement in patients with rectal cancer: a systematic review and meta-analysis. *Ann Surg Oncol*. 2012 Jul; 19(7): 2212-23.
7. Arii K, Takifuji K, Yokoyama S, et al. Preoperative evaluation of pelvic lateral lymph node of patients with lower rectal cancer: comparison study of MR imaging and CT in 53 patients. *Langenbecks Arch Surg*. 2006 Sep; 391(5): 449-54.
8. Matsuoka H, Nakamura A, Masaki T, et al. Optimal diagnostic criteria for lateral pelvic lymph node metastasis in rectal carcinoma. *Anticancer Res*. 2007 Sep; 27(5B): 3529-33.
9. Akasu T, Iinuma G, Takawa M, et al. Accuracy of high-resolution magnetic resonance imaging in preoperative staging of rectal cancer. *Ann Surg Oncol*. 2009 Oct; 16(10): 2787-94.
10. Ishibe A, Ota M, Watanabe J, et al. Prediction of lateral pelvic lymph-node metastasis in low rectal cancer by magnetic resonance imaging. *World J Surg*. 2016 Apr; 40(4): 995-1001.
11. Ogawa S, Hida J, Ike H, 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 Apr; 23(4): 1187-94.
12. Ishida H, Hatano S, Ishiguro T, et al. Prediction of lateral lymph node metastasis in lower rectal cancer: analysis of paraffin-embedded sections. *Jpn J Clin Oncol* 2012 Mar; 42(6): 485-90.
13. Lu YY, Chen JH, Ding HJ, et al. A systematic review and meta-analysis of pretherapeutic lymph node staging of colorectal cancer by 18F-FDG PET or PET/CT. *Nucl Med Commun*. 2012 Nov; 33(11): 1127-33.

14. Hatano S, Ishida H, Ishiguro T, et al. Prediction of metastasis to mesorectal, internal iliac and obturator lymph nodes according to size criteria in patients with locally advanced lower rectal cancer. *Jpn J Clin Oncol*. 2014 Oct; 45(1): 35-42.
15. Japanese Society for Cancer of the Colon and Rectum. Japanese Classification of Colorectal Carcinoma. 8th ed. Tokyo: Kanehara; 2013.
16. Brown G, Richards CJ, Bourne MW, et al. Morphologic predictors of lymph node status in rectal cancer with use of high-spatial-resolution MR imaging with histopathologic comparison. *Radiology*. 2003 May; 227(2): 371-7.
17. Bipat S, Glas AS, Slors FJ, et al. Rectal cancer: local staging and

assessment of lymph node involvement with endoluminal US, CT, and MR imaging—a meta-analysis. *Radiology*. 2004 Sep; 232(3): 773-83.

#### Supplementary File

**Supplementary Figure 1.** Pathological characteristics of each LPLNs with false negative (magnification, x4).

Journal of the Anus, Rectum and Colon is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).