**Name of Journal:** *World Journal of Clinical Oncology*

**Manuscript NO:** 87811

**Manuscript Type:** MINIREVIEWS

**Current perspectives on the management of lateral pelvic lymph nodes in rectal cancer**

Chua JYJ *et al*. Review of PLND in rectal cancer

Jonathan Yu Jin Chua, James Chi Yong Ngu, Nan Zun Teo

**Jonathan Yu Jin Chua, James Chi Yong Ngu, Nan Zun Teo,** Department of General Surgery, Changi General Hospital, Singapore 529889, Singapore

**Author contributions:** Chua JYJ drafted the article; Ngu JCY and Teo NZ were involved in the concept and design of the article, critical revision, and final approval.

**Corresponding author: Nan Zun Teo,** Department of General Surgery, Changi General Hospital, 2 Simei Street 3, Singapore 529889, Singapore. teo.nan.zun@singhealth.com.sg

**Received:** August 28, 2023

**Revised:** November 7, 2023

**Accepted:** November 24, 2023

**Published online:**

**Abstract**

Significant controversies exist with regards to the optimal management of lateral pelvic lymph nodes metastases (mLLN) in patients with low rectal cancer. The differing views held by Japanese and Western clinicians on the management of mLLN have been well documented. However, the adequacy of pelvic lymph node dissection (PLND) or neoadjuvant chemoradiation (NACRT) alone in addition to total mesorectal excision (TME) have recently come into question, due to the relatively high incidence of lateral local recurrences following PLND and TME, or NACRT and TME alone. Recently, a more selective approach to PLND has been suggested, involving a combination of neoadjuvant therapy, followed by PLND only to patients in whom the oncological benefit is likely to outweigh the risk of potential adverse events. A number of studies have attempted to retrospectively identify certain nodal characteristics on preoperative imaging, such as nodal size, appearance, and size reduction following neoadjuvant therapy. However, no consensus has been reached regarding the optimal criteria for a selective approach to PLND, partly due to the heterogeneity and retrospective nature of most of these studies. This review aims to provide an overview of recent evidence with regards to the diagnostic challenges, considerations for, and outcomes of the current management strategies for mLLN in rectal cancer patients.

**Key Words:** Pelvic lymph node dissection; Lateral pelvic lymph nodes; Diagnostic criteria; Short axis diameter; Radiotherapy; Rectal cancer

Chua JYJ, Ngu JCY, Teo NZ. Current perspectives on the management of lateral pelvic lymph nodes in rectal cancer. *World J Clin Oncol* 2023; In press

**Core Tip:** The optimal management strategy for lateral pelvic lymph node metastases (mLLN) requires a multimodal approach, involving chemoradiation and pelvic lymph node dissection (PLND), in order to achieve adequate local control in patients with locally advanced low rectal cancer. This selective approach requires careful selection of patients who would benefit most from PLND, using pre-treatment nodal short axis measurements as a surrogate for mLLN risk.

**INTRODUCTION**

Total mesorectal excision (TME) and the circumferential resection margin have been widely accepted as crucial elements in the surgical treatment of rectal cancer. However, the management of pelvic side wall disease remains controversial, and historically divergent between countries in the West and those in the far East. While the former predominantly recommend the use of radiotherapy (with or without chemotherapy), pelvic lymph node dissection (PLND) is preferred in the latter. This has been reflected in guidelines published by their respective societies[1-3].

Results from the Dutch TME trial[4] (10-year local recurrence (LR) rates of 5% in the irradiated group *vs* 11% in the non-irradiated group, *P* < 0.0001) and the Swedish Rectal Cancer Trial[5] (LR rate of 9% in the irradiated group *vs* 26% in the non-irradiated group, *P* < 0.001) supported the use of neoadjuvant radiotherapy. These rates were comparable to patients who underwent PLND in some Japanese studies. In contrast, early results of PLND in the West[6,7] were discouraging due to high perioperative morbidity and limited reported oncological benefit[8], resulting in its slow uptake.

In Japan, however, lower local failure rates (Dukes B cases 8.4% *vs* 26.1%, *P* < 0.01, Dukes C cases 24.5% *vs* 44.3%, *P* < 0.01) and improved 5-year survival (Dukes B cases 83.2% *vs* 63.7%, *P* < 0.05; Dukes C cases 52.5% *vs* 30.8%, *P* < 0.05) were reported when extended lymphadenectomy was performed[9]. In addition, PLND was only associated with a slight prolongation of operating time (additional 60 min), a modest increase in operative blood loss (additional 150 mL), and no increase in operative mortality[9].

This article aims to elucidate the factors contributing to the contrasting recommendations in the management of lateral pelvic lymph nodes (LLN), and to provide a more contemporary approach to this conundrum. Literature search was performed electronically using PubMed (MEDLINE) and the *Reference Citation Analysis* (https://www.referencecitationanalysis.com) was applied. The search terms were as follows: pelvic lymph node dissection or PLND, lateral lymph node metastasis, and rectal cancer in combination with Boolean operators AND and OR. All studies in English were extracted for review by the authors.

**THE SIGNIFICANCE OF THE LATERAL PELVIC LYMPH NODES**

The difference in lymphatic drainage of the lower rectum from the upper rectum has been well documented, with Gerota[10] describing how tumours in the mid and lower rectum appear to exhibit lateral lymphatic drainage into the iliac nodes in addition to upward drainage through mesorectal nodes[11,12].

The risk of developing lateral lymph node metastases (mLLN) in rectal cancer has been shown to vary with several factors. Distance from the anal verge has been reported to be inversely related to the risk of mLLN, with rates of up to 33.3% observed in tumours ≤ 3.9cm from the anal verge[13]. Locally advanced pT3 and pT4 tumours tend to also be associated with higher rates of mLLN[13]. In particular, it has been demonstrated that mLLN were mostly located in the group of nodes along the internal iliac artery (IIA), being the first draining basin from the lateral rectal ligaments[14-16].

Traditional TNM staging for rectal cancer classifies malignant deposits in the external iliac and obturator nodes as distant metastases[17]. On the other hand, the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma (3rd edition)[18], includes lymph nodes along the IIA, obturator, external iliac, common iliac (CIA), and median sacral arteries within its definition of regional lymph nodes, in the context of lower rectal cancers. This was based on survival data from the Japanese Nationwide Multi-Institutional Study on Lateral Pelvic Lymph Node Metastasis in Low Rectal Cancer[19]. Patients with metastasis to the above, so-called external lateral pelvic nodes, demonstrated more favourable overall survival and cancer-specific survival if they underwent PLND, than in patients with stage IV disease who underwent R0 resection (overall survival 29% *vs* 24%, *P* = 0.0240, cancer-specific survival 37% *vs* 27%, *P* = 0.0117). In addition, Ogura *et al*[20] determined that LLN enlargement did not appear to influence distant recurrence rate, suggesting that mLLN likely represent locoregional disease.

**diagnostic dilemmas – diagnostic criteria, misdiagnosis and missed diagnoses**

However, epidemiological studies on mLLN suffer from the heterogenous methods used in evaluating nodal disease, with incidence rates being reported to range between 8.8% and 34%[13,21]. Studies that do not involve PLND would base their diagnosis on imaging, whereas analyses involving patients who had undergone PLND would report based on pathological confirmation. Most studies that evaluate recurrences in the pelvic side wall do so by means of imaging parameters.

The main challenge in preoperative radiological assessment of LLN lies in not missing occult metastases within the nodes (missed diagnoses), while minimising cases of misdiagnoses. Most imaging modalities have been evaluated for their diagnostic accuracy in detecting suspicious lateral pelvic nodes. Ultrasonography was suggested as a potential imaging modality for this purpose, but failed to adequately examine obturator nodes[22], and has largely been surpassed by other imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). Even then, the sensitivity of CT and MRI in detecting mLLN varies greatly between studies[23,24]. More recently, the accuracy of F-fluorodeoxyglucose positron-emission tomography (18F-FDG PET) as a diagnostic adjunct in addition to CT or MRI has also been evaluated, although many guidelines do not include 18F-FDG PET scanning as part of the initial staging for rectal cancer patients[2,25]. A study by Ishihara *et al*[26] evaluated the accuracy of 18F-FDG PET scanning in identifying suspicious LLN post neoadjuvant chemotherapy, using a calculated maximum standard uptake value (SUV max) of 1.6, and reported an accuracy, sensitivity, and specificity of 85.7%, 76.5%, and 100% respectively. Metastatic LLN were found to have a significantly higher SUV max when compared to LLN without metastatic deposits (mean ± standard deviation 2.2 ± 1.3 *vs* 1.2 ± 0.3, *P* < 0.01). A similar study by Yukimoto *et al*[27] subsequently reported similar values (accuracy 92.3%, sensitivity 82.4%, specificity 93.4%) with a slightly lower SUVmax cutoff value of 1.5. These studies were mainly limited due to their small cohort size, and the utility of 18F-FDG PET scanning in rectal cancer in most units has been mainly limited to the evaluation of equivocal findings on contrast-enhanced CT, or in patients with a strong contraindication to intravenous contrast[3]. As a result, the European Society for Medical Oncology and the American Society of Colon and Rectal Surgeons still recommend the use of pelvic MRI for locoregional staging[2,25].

Apart from the type of imaging modality, there also exists a lack of consensus in what imaging features constitute a suspicious LLN, or mLLN. Table 1 summarises the various criteria used. Most studies retrospectively identify short (SAD), or long axis diameter (LAD) measurements and nodal features that correlate with pathological nodal metastases and/or oncological outcome. The multi-national Society of Abdominal Radiology – Rectal & Anal Cancer Disease-Focused Panel recently published a consensus statement[28] to promote consistent terminology and reporting standards amongst abdominal radiologists. The consensus statement recommended internal iliac and obturator nodes with SAD > 7 mm be reported as suspicious[28]. The MERCURY[29] study reviewed the preoperative MRI images of patients with biopsy-proven rectal adenocarcinoma within 15cm from the anal verge who underwent TME without PLND. The nodes were considered suspicious based on the presence of mixed signal intensity and/or an irregular nodal capsule border.

Further contributing to the heterogeneity is the inconsistent use of pre- or post-neoadjuvant imaging, or a combination of both sets of imaging (reflecting the response to neoadjuvant treatment). Akiyoshi *et al*[30] showed that the incidence of occult mLLN was as high as 20% even in patients with a post-neoadjuvant nodal size of 5 mm or less, supporting the recommendation of basing further treatment selection on pre-neoadjuvant imaging.

With regards to post-neoadjuvant nodal size, Cribb *et al*[31] found that a SAD of ≥ 5 mm on post-treatment MRI was associated with a worse 3-year local recurrence-free survival [hazard ratio (HR) 8.35, *P* = 0.001]. Malakorn *et al*[32] concluded that a post-neoadjuvant nodal size of ≥ 5 mm was 100% sensitive for identifying patients with mLLN and as such recommend using a post-neoadjuvant LLN size cutoff of 5 mm for PLND. The high reported sensitivity of a post-treatment nodal SAD of ≥ 5 mm is promising and has been recommended as suitable criteria for PLND[32,33]. In addition, the Lateral Node Study Consortium demonstrated that PLND can be safely omitted in patients with LLN measuring 4mm or less on restaging MRI due to the negligible risk of lateral local recurrence at 3 years in this subgroup of patients[14].

Akiyoshi *et al*[30] analysed patients with cT3/4 rectal cancers who underwent either bilateral (15.6%) or unilateral (84.4%) PLND, based on a nodal LAD cutoff of ≥ 7 mm on pre-neoadjuvant CT or MRI. Pathological mLLN were found in 40.3% of patients, and persistent LLN on restaging was associated with a higher rate of metastatic deposits when compared with LLN that responded to neoadjuvant chemoradiotherapy (CRT) (75% *vs* 20%, *P* < 0.0001)[30].

In publications reporting pathological results, incidence rates can also be confounded by potential missed diagnoses. The identification of micrometastatic disease or isolated tumour cells may sometimes pose a diagnostic challenge. Miyake *et al*[34] compared the sensitivity of one-step nucleic acid amplification assay results to conventional histological diagnosis, and identified a number of additional histologically-negative nodes with metastatic disease. Limitations in commonly utilised histological processing methods may have resulted in a small proportion of missed diagnoses of mLLN, with failure to pathologically upstage such patients resulting in adverse prognostic implications.

**The adequacy of PLND or/and Chemoradiation**

While the efficacy of neoadjuvant CRT in reducing LR rates have been well documented[4,5], lateral pelvic recurrences have nonetheless been reported in cases where PLND was omitted after CRT[35]. Kim *et al*[36] reported a 64.6% lateral local recurrence (LLR) rate, out of a 7.2% LR rate following pre or post-operative chemoradiotherapy, after a median follow-up period of 65 mo. Kusters *et al*[37] similarly reported a 64.3% LLR rate and 18.7% LR rate. Both studies concluded that LLN measuring ≥ 10 mm were associated with an increased risk of recurrence and poorer overall survival, and that CRT alone in these patients did not confer adequate local control.

On the other hand, the Japanese JCOG0212[38-40] randomised controlled trial illustrated the impact of bilateral prophylactic PLND alone, without the use of CRT, even though adjuvant chemotherapy was prescribed to pathological stage III patients. Only patients without clinically suspicious LLN nodes (SAD ≥ 10 mm on CT/MRI) were enrolled. The study reported that the addition of PLND resulted in a statistically significant reduction in LR rates (7.4% *vs* 12.6%, *P* = 0.024), and a higher local recurrence-free survival of 85.3%, compared to 80.3% with TME alone. The authors therefore concluded that the trial failed to demonstrate the noninferiority of TME alone, even though the significant reduction in LR may have resulted from the SAD cutoff of 10mm being insufficiently sensitive in predicting for mLLN. Nonetheless, the 7% incidence of occult mLLN in this trial suggests that a significant proportion of patients were subjected to the morbidity of PLND without deriving any oncological benefit.

Other studies evaluated the impact of combining the two treatment modalities. Kim *et al*[35] retrospectively analysed 366 patients with cT3/4 tumours within 8 cm from the anal verge who received CRT prior to TME without PLND. They reported a LR rate of 7.9% after a median follow-up duration of 40.1 mo, with 82.7% of these being LLR. Conversely, the addition of PLND to TME significantly reduced LR rates despite prior CRT (CRT+TME 19.5% *vs* CRT+TME+PLND 5.7%, *P* = 0.042)[20].

A three-armed multinational study by Kusters *et al*[41] compared patients with rectal cancer from the Netherlands and Japan who underwent either (1) TME alone; (2) TME with (neo)adjuvant radiation; or (3) TME with PLND. Similar overall LR rates were reported between groups (2) and (3) (RT+TME 5.8% *vs* 6.9% PLND+TME, HR 1.0 (0.6-1.8). Only group (1) had a higher 5-year LR rate of 12.1%.

Recently, a multicentre retrospective study by Ogura *et al*[14] found that nodes along the internal iliac artery were less responsive to chemoradiation, and concluded that IIA nodes measuring 7 mm or more on pre-treatment MRI were predictors of lateral local recurrence. The study reported 5-year LLR rates of 52.3% following neoadjuvant chemoradiotherapy and TME surgery but without PLND[14]. When PLND was performed, the 5-year LLR risk was significantly reduced to 8.7% (*P* = 0.007)[14].

**SELECTIVE PLND post neoadjuvant radiotherapy**

The optimal management of mLLN appears to therefore be shifting towards a selective multimodal approach, with selective PLND post neoadjuvant therapy appearing to offer higher rates of local control in several studies. Numerous variables have been proposed as potential indications for PLND due to their reported sensitivities in identifying occult mLLN, and their prognostic implications. In addition to the aforementioned studies, Akiyoshi *et al*[42] reviewed patients with stage II-III low rectal cancer who underwent preoperative CRT prior to surgery. PLND was performed in patients with suspicious LLN on pre-neoadjuvant CT or MRI, using SAD criteria of ≥ 7 mm[42]. Patients with clinically enlarged LLN underwent PLND irrespective of findings on post-treatment restaging[42]. The study observed that no LLR occurred in patients who underwent PLND, while 3.4% of patients who only underwent TME post chemoradiation developed LLR[42]. A similar study by Ishihara *et al*[43] reported similar findings. PLND was again performed based on the presence of suspicious pre-neoadjuvant nodes, irrespective of their response to neoadjuvant treatment[43]. The study reported LLR rates of 0% and 0.9% in patients who underwent TME with PLND and TME only respectively[43], suggesting that the selective addition of PLND is key in achieving local control in the lateral pelvis. Therefore, suspicious internal iliac or obturator nodes with pre-treatment SAD of ≥ 7 mm, or the presence of nodes displaying heterogeneity and/or irregular borders, should form indications for PLND.

**TECHNICAL CHALLENGES OF PLND**

In the treatment of rectal cancer, PLND typically involves removal of nodes in the internal iliac and obturator compartments[44]. The JCOG0212 trial concluded that the addition of PLND was associated with a significantly longer operative time (median 360 min *vs* 254 min, *P* < 0.0001) when compared to TME alone, and was associated with more intraoperative blood loss (576 mL *vs* 337 mL, *P* < 0.0001)[45]. No statistically significant differences were reported with regards to the incidence of anastomotic leakage (*P* = 0.46), urinary retention (*P* = 0.18), wound infection (*P* = 0.81), pelvic abscess (*P* = 0.29), or bowel obstruction (*P* = 1.00)[45]. A meta-analysis of extended lymphadenectomy *vs* conventional surgery for rectal cancer found similar results, with no significant differences in perioperative mortality (*P* = 0.63) or morbidity (*P* = 0.13)[46].

In a bid to promote the safe implementation of PLND, Ngu *et al*[47] conceptualised the use of origami to convert the pelvic side wall from a 2-dimensional region into a 3-dimensional compartment made up of two triangular pyramids. The authors sought to simplify PLND into a procedure involving three planes, three boundaries, and three steps. The three planes consisted of the (1) ureterohypogastric nerve fascia (UHNF); the (2) vesicohypogastric fascia; and (3) the external iliac muscular plane. Following medialisation of the UHNF, the proximal boundary is marked by two key landmarks: superficially where the ureter crosses the CIA and, at a deeper plane, the bifurcation of the common iliac vein, where the obturator nerve enters the pelvic sidewall compartment. The distal boundary is delineated superficially by the vas deferens or round ligament, and, at a deeper level, the obturator foramen. The third (deep) boundary is marked by the terminal branches of the internal iliac vessels. The three steps of PLND involve (1) the separation of these three planes, followed by (2) the delineation of the three boundaries, and finally (3) the dissection of the internal iliac vessels, with en bloc removal of the lympho-fatty tissue.

Tang *et al*[48] compared the short-term outcomes of laparoscopic PLND against open PLND, and concluded that laparoscopic PLND was associated with a shorter operative time (255 min *vs* 300 min, *P* = 0.001), less intraoperative blood loss (50 mL *vs* 300 mL, *P* < 0.001), lower incidence of postoperative complications (32% *vs* 15%, *P* = 0.005), shorter postoperative hospital stay (8 *vs* 14 d, *P* < 0.001), and excision of more lateral pelvic nodes (9 *vs* 7 nodes, *P* = 0.025) when compared to open PLND. Oncological outcomes were similar, with no differences reported in 3-year overall survival (*P* = 0.581) and disease-free survival (*P* = 0.745) rates[48]. Aside from the aforementioned postoperative complications, this study also reported other surgical complications such as chylous ascites and lower limb neuropathy, as well as systemic complications such as renal failure, pneumonia, and arrhythmias[48].

Utilization of the robotic platform in PLND has recently been shown to result in lower blood loss (25 mL *vs* 637 mL, *P* < 0.0001) and less postoperative complications including wound infection, anastomotic leakage, urinary retention, and small bowel obstruction when compared to open PLND, but operative times were longer (455 min *vs* 410 min, *P* < 0.007)[49]. Robotic PLND was also associated with superior 5-year local relapse-free survival rates compared to open PLND (98.6% *vs* 90.9%, *P* = 0.029), with similar overall survival (robotic 95.4% *vs* open 87.8%, *P* = 0.106) and relapse-free survival rates (robotic 79.1% *vs* open 69.9%, *P* = 0.157)[50]. Although PLND is a technically demanding procedure with significant risk of associated morbidity, robotic or laparoscopic assistance may be useful adjuncts, associated with lower postoperative morbidity rates when performed by experienced surgeons.

Although not traditionally a recordable perioperative morbidity, the potential of missed nodes during PLND may result in poorer oncological outcomes. A novel strategy to potentially mitigate the risk of intraoperatively missed nodes during PLND is the utilisation of indocyanine green (ICG) during laparoscopic PLND[51,52]. Ohya *et al*[52] conducted a retrospective study of patients who underwent PLND for tumours cT3 and above with clinically suspicious lateral pelvic nodes on pre-op imaging. The study demonstrated an increased lymph node yield (ICG 14 *vs* no ICG 9, *P* < 0.001), without a substantial difference in post-operative complications (*P* = 0.57), aside from a longer operative time (ICG 426 min *vs* no-ICG 369 min, *P* < 0.001). ICG use was also associated with a significant reduction in intraoperative blood loss (13 mL *vs* 100 mL, *P* = 0.001). The authors recently published their long-term follow-up data, and the higher lymph node yield with ICG translated into a reduction in 3-year cumulative LR rates (ICG 0% *vs* no-ICG 9.3%, *P* = 0.048), although no statistically significant difference was reported in relapse-free survival and overall survival rates[51].

**CONCLUSION**

The difficulty in reaching a global consensus with regards to the optimal management of LLN in rectal cancer stems from the heterogeneity of available data, mainly consisting of retrospective cohort studies using various parameters to define what constitutes a clinically suspicious LLN, or mLLN. Contemporary data appears to suggest that the optimal strategy may lie somewhere between the traditional views held by Western countries and the far East. Several conclusions can be drawn from the existing data: Firstly, pelvic lymph node dissection in rectal cancer has to offered selectively. The JCOG0212[38-40] study demonstrated that in the absence of radiologically suspicious nodes, the majority of patients would not benefit from PLND, hence justifying a more selective, non-prophylactic approach to PLND. Secondly, the optimal management strategy for mLLN in patients with rectal cancer requires a multimodal approach, involving a combination of neadjuvant chemoradiation and selective PLND. Thirdly, until more robust data is made available, a prudent choice would be to use a SAD of ≥ 7 mm, or the presence of suspicious features, as criteria for selective PLND. This assessment should be made based on pre-neoadjuvant MRI.

**REFERENCES**

1 **Hashiguchi Y**, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T, Hasegawa K, Hotta K, Ishida H, Ishiguro M, Ishihara S, Kanemitsu Y, Kinugasa Y, Murofushi K, Nakajima TE, Oka S, Tanaka T, Taniguchi H, Tsuji A, Uehara K, Ueno H, Yamanaka T, Yamazaki K, Yoshida M, Yoshino T, Itabashi M, Sakamaki K, Sano K, Shimada Y, Tanaka S, Uetake H, Yamaguchi S, Yamaguchi N, Kobayashi H, Matsuda K, Kotake K, Sugihara K; Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. *Int J Clin Oncol* 2020; **25**: 1-42 [PMID: 31203527 DOI: 10.1007/s10147-019-01485-z]

2 **Glynne-Jones R**, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A, Arnold D; ESMO Guidelines Committee. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2017; **28**: iv22-iv40 [PMID: 28881920 DOI: 10.1093/annonc/mdx224]

3 **Benson AB**, Venook AP, Al-Hawary MM, Azad N, Chen YJ, Ciombor KK, Cohen S, Cooper HS, Deming D, Garrido-Laguna I, Grem JL, Gunn A, Hecht JR, Hoffe S, Hubbard J, Hunt S, Jeck W, Johung KL, Kirilcuk N, Krishnamurthi S, Maratt JK, Messersmith WA, Meyerhardt J, Miller ED, Mulcahy MF, Nurkin S, Overman MJ, Parikh A, Patel H, Pedersen K, Saltz L, Schneider C, Shibata D, Skibber JM, Sofocleous CT, Stotsky-Himelfarb E, Tavakkoli A, Willett CG, Gregory K, Gurski L. Rectal Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2022; **20**: 1139-1167 [PMID: 36240850 DOI: 10.6004/jnccn.2022.0051]

4 **van Gijn W**, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, Rutten HJ, Påhlman L, Glimelius B, van de Velde CJ; Dutch Colorectal Cancer Group. 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; **12**: 575-582 [PMID: 21596621 DOI: 10.1016/S1470-2045(11)70097-3]

5 **Folkesson J**, Birgisson H, Pahlman L, Cedermark B, Glimelius B, Gunnarsson U. Swedish Rectal Cancer Trial: long lasting benefits from radiotherapy on survival and local recurrence rate. *J Clin Oncol* 2005; **23**: 5644-5650 [PMID: 16110023 DOI: 10.1200/JCO.2005.08.144]

6 **Sauer I**, BACON HE. Influence of lateral spread of cancer of the rectum on radicability of operation and prognosis. *Am J Surg* 1951; **81**: 111-120 [PMID: 14799702 DOI: 10.1016/0002-9610(51)90196-1]

7 **Stearns MW Jr**, DEDDISH MR. Five-year results of abdominopelvic lymph node dissection for carcinoma of the rectum. *Dis Colon Rectum* 1959; **2**: 169-172 [PMID: 13652786 DOI: 10.1007/BF02616711]

8 **Williamson JS**, Quyn AJ, Sagar PM. Rectal cancer lateral pelvic sidewall lymph nodes: a review of controversies and management. *Br J Surg* 2020; **107**: 1562-1569 [PMID: 32770742 DOI: 10.1002/bjs.11925]

9 **Koyama Y**, Moriya Y, Hojo K. Effects of extended systematic lymphadenectomy for adenocarcinoma of the rectum--significant improvement of survival rate and decrease of local recurrence. *Jpn J Clin Oncol* 1984; **14**: 623-632 [PMID: 6520971]

10 **Gerota D.** Die Lymphgefasse des Rectums und des Anus. *Arch Anat Physiol* 1895

11 **Zhou S**, Jiang Y, Pei W, Liang J, Zhou Z. Prognostic significance of lateral pelvic lymph node dissection for middle-low rectal cancer patients with lateral pelvic lymph node metastasis: a propensity score matching study. *BMC Cancer* 2022; **22**: 136 [PMID: 35109810 DOI: 10.1186/s12885-022-09254-4]

12 **SAUER I**, BACON HE. A new approach for excision of carcinoma of the lower portion of the rectum and anal canal. *Surg Gynecol Obstet* 1952; **95**: 229-242 [PMID: 14950656]

13 **Morikawa E**, Yasutomi M, Shindou K, Matsuda T, Mori N, Hida J, Kubo R, Kitaoka M, Nakamura M, Fujimoto K. Distribution of metastatic lymph nodes in colorectal cancer by the modified clearing method. *Dis Colon Rectum* 1994; **37**: 219-223 [PMID: 8137667 DOI: 10.1007/BF02048158]

14 **Ogura A**, Konishi T, Beets GL, Cunningham C, Garcia-Aguilar J, Iversen H, Toda S, Lee IK, Lee HX, Uehara K, Lee P, Putter H, van de Velde CJH, Rutten HJT, Tuynman JB, Kusters M; Lateral Node Study Consortium. 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**: e192172 [PMID: 31268504 DOI: 10.1001/jamasurg.2019.2172]

15 **Kanemitsu Y**, Komori K, Shida D, Ochiai H, Tsukamoto S, Kinoshita T, Moriya Y. Potential impact of lateral lymph node dissection (LLND) for low rectal cancer on prognoses and local control: A comparison of 2 high-volume centers in Japan that employ different policies concerning LLND. *Surgery* 2017; **162**: 303-314 [PMID: 28366499 DOI: 10.1016/j.surg.2017.02.005]

16 **Takahashi T**, Ueno M, Azekura K, Ohta H. Lateral node dissection and total mesorectal excision for rectal cancer. *Dis Colon Rectum* 2000; **43**: S59-S68 [PMID: 11052480 DOI: 10.1007/BF02237228]

17 **Brierley JD,** Gospodarowicz MK, Wittekind C, editors. TNM Classification of Malignant Tumours, 8th Edition. *Wiley-Blackwell* 2016; 73–76

18 **Japanese Society for Cancer of the Colon and Rectum**. Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma: the 3d English Edition [Secondary Publication]. *J Anus Rectum Colon* 2019; **3**: 175-195 [PMID: 31768468 DOI: 10.23922/jarc.2019-018]

19 **Akiyoshi T**, Watanabe T, Miyata S, Kotake K, Muto T, Sugihara K; Japanese Society for Cancer of the Colon and Rectum. Results of a Japanese nationwide multi-institutional study on lateral pelvic lymph node metastasis in low rectal cancer: is it regional or distant disease? *Ann Surg* 2012; **255**: 1129-1134 [PMID: 22549752 DOI: 10.1097/SLA.0b013e3182565d9d]

20 **Ogura A**, Konishi T, Cunningham C, Garcia-Aguilar J, Iversen H, Toda S, Lee IK, Lee HX, Uehara K, Lee P, Putter H, van de Velde CJH, Beets GL, Rutten HJT, Kusters M; Lateral Node Study Consortium. 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**: 33-43 [PMID: 30403572 DOI: 10.1200/JCO.18.00032]

21 **Peacock O**, Manisundaram N, Dibrito SR, Kim Y, Hu CY, Bednarski BK, Konishi T, Stanietzky N, Vikram R, Kaur H, Taggart MW, Dasari A, Holliday EB, You YN, Chang GJ. Magnetic Resonance Imaging Directed Surgical Decision Making for Lateral Pelvic Lymph Node Dissection in Rectal Cancer After Total Neoadjuvant Therapy (TNT). *Ann Surg* 2022; **276**: 654-664 [PMID: 35837891 DOI: 10.1097/SLA.0000000000005589]

22 **Tada M**, Endo M. Ultrasonographic examination for lateral lymphatic spread and local recurrence of rectal cancer. Preoperative detection and evaluation. *Dis Colon Rectum* 1995; **38**: 1047-1052 [PMID: 7555418 DOI: 10.1007/BF02133977]

23 **Amano K**, Fukuchi M, Kumamoto K, Hatano S, Ohno H, Osada H, Ishibashi K, Ishida H. Pre-operative Evaluation of Lateral Pelvic Lymph Node Metastasis in Lower Rectal Cancer: Comparison of Three Different Imaging Modalities. *J Anus Rectum Colon* 2020; **4**: 34-40 [PMID: 32002474 DOI: 10.23922/jarc.2019-022]

24 **Numata K**, Katayama Y, Sawazaki S, Higuchi A, Morinaga S, Rino Y, Masuda M, Shiozawa M. Utility of Preoperative Imaging for Predicting Pelvic Lateral Lymph Node Metastasis in Lower Rectal Cancer. *Indian J Surg Oncol* 2019; **10**: 582-586 [PMID: 31857748 DOI: 10.1007/s13193-019-00947-0]

25 **You YN**, Hardiman KM, Bafford A, Poylin V, Francone TD, Davis K, Paquette IM, Steele SR, Feingold DL; On Behalf of the Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Rectal Cancer. *Dis Colon Rectum* 2020; **63**: 1191-1222 [PMID: 33216491 DOI: 10.1097/DCR.0000000000001762]

26 **Ishihara S**, Kawai K, Tanaka T, Kiyomatsu T, Hata K, Nozawa H, Morikawa T, Watanabe T. Diagnostic value of FDG-PET/CT for lateral pelvic lymph node metastasis in rectal cancer treated with preoperative chemoradiotherapy. *Tech Coloproctol* 2018; **22**: 347-354 [PMID: 29623475 DOI: 10.1007/s10151-018-1779-0]

27 **Yukimoto R**, Uemura M, Tsuboyama T, Hata T, Fujino S, Ogino T, Miyoshi N, Takahashi H, Hata T, Yamamoto H, Mizushima T, Kida A, Furuyashiki M, Doki Y, Eguchi H. Efficacy of positron emission tomography in diagnosis of lateral lymph node metastases in patients with rectal Cancer: a retrospective study. *BMC Cancer* 2021; **21**: 520 [PMID: 33962569 DOI: 10.1186/s12885-021-08278-6]

28 **Lee S**, Kassam Z, Baheti AD, Hope TA, Chang KJ, Korngold EK, Taggart MW, Horvat N. Rectal cancer lexicon 2023 revised and updated consensus statement from the Society of Abdominal Radiology Colorectal and Anal Cancer Disease-Focused Panel. *Abdom Radiol (NY)* 2023; **48**: 2792-2806 [PMID: 37145311 DOI: 10.1007/s00261-023-03893-2]

29 **MERCURY Study Group**, Shihab OC, Taylor F, Bees N, Blake H, Jeyadevan N, Bleehen R, Blomqvist L, Creagh M, George C, Guthrie A, Massouh H, Peppercorn D, Moran BJ, Heald RJ, Quirke P, Tekkis P, Brown G. Relevance of magnetic resonance imaging-detected pelvic sidewall lymph node involvement in rectal cancer. *Br J Surg* 2011; **98**: 1798-1804 [PMID: 21928408 DOI: 10.1002/bjs.7662]

30 **Akiyoshi T**, Matsueda K, Hiratsuka M, Unno T, Nagata J, Nagasaki T, Konishi T, Fujimoto Y, Nagayama S, Fukunaga Y, Ueno M. 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; **22 Suppl 3**: S614-S620 [PMID: 25896145 DOI: 10.1245/s10434-015-4565-5]

31 **Cribb BI**, Kong JC, Kay JS, Tan TH, Noe GD, Gest B, Lee AB, Oon SF, Warrier SK, Heriot AG. Metabolic and magnetic resonance imaging: complementary modalities for the preoperative assessment of lateral pelvic lymph nodes in rectal cancer. *ANZ J Surg* 2023; **93**: 196-205 [PMID: 36074654 DOI: 10.1111/ans.18020]

32 **Malakorn S**, Yang Y, Bednarski BK, Kaur H, You YN, Holliday EB, Dasari A, Skibber JM, Rodriguez-Bigas MA, Chang GJ. Who Should Get Lateral Pelvic Lymph Node Dissection After Neoadjuvant Chemoradiation? *Dis Colon Rectum* 2019; **62**: 1158-1166 [PMID: 31490825 DOI: 10.1097/DCR.0000000000001465]

33 **Peacock O**, Chang GJ. The Landmark Series: Management of Lateral Lymph Nodes in Locally Advanced Rectal Cancer. *Ann Surg Oncol* 2020; **27**: 2723-2731 [PMID: 32519144 DOI: 10.1245/s10434-020-08639-8]

34 **Miyake Y**, Mizushima T, Hata T, Takahashi H, Hanada H, Shoji H, Nomura M, Haraguchi N, Nishimura J, Matsuda C, Takemasa I, Doki Y, Maeda I, Mori M, Yamamoto H. Inspection of Perirectal Lymph Nodes by One-Step Nucleic Acid Amplification Predicts Lateral Lymph Node Metastasis in Advanced Rectal Cancer. *Ann Surg Oncol* 2017; **24**: 3850-3856 [PMID: 28924845 DOI: 10.1245/s10434-017-6069-y]

35 **Kim TH**, Jeong SY, Choi DH, Kim DY, Jung KH, Moon SH, Chang HJ, Lim SB, Choi HS, 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* 2008; **15**: 729-737 [PMID: 18057989 DOI: 10.1245/s10434-007-9696-x]

36 **Kim MJ**, Kim TH, Kim DY, Kim SY, Baek JY, Chang HJ, Park SC, Park JW, Oh JH. Can chemoradiation allow for omission of lateral pelvic node dissection for locally advanced rectal cancer? *J Surg Oncol* 2015; **111**: 459-464 [PMID: 25559888 DOI: 10.1002/jso.23852]

37 **Kusters M**, Slater A, Muirhead R, Hompes R, Guy RJ, Jones OM, George BD, Lindsey I, Mortensen NJ, Cunningham C. What To Do With Lateral Nodal Disease in Low Locally Advanced Rectal Cancer? A Call for Further Reflection and Research. *Dis Colon Rectum* 2017; **60**: 577-585 [PMID: 28481851 DOI: 10.1097/DCR.0000000000000834]

38 **Fujita S**, Mizusawa J, Kanemitsu Y, Ito M, Kinugasa Y, Komori K, Ohue M, Ota M, Akazai Y, Shiozawa M, Yamaguchi T, Bandou H, Katsumata K, Murata K, Akagi Y, Takiguchi N, Saida Y, Nakamura K, Fukuda H, Akasu T, Moriya Y; Colorectal Cancer Study Group of Japan Clinical Oncology Group. 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**: 201-207 [PMID: 28288057 DOI: 10.1097/SLA.0000000000002212]

39 **Tsukamoto S**, Fujita S, Ota M, Mizusawa J, Shida D, Kanemitsu Y, Ito M, Shiomi A, Komori K, Ohue M, Akazai Y, Shiozawa M, Yamaguchi T, Bando H, Tsuchida A, Okamura S, Akagi Y, Takiguchi N, Saida Y, Akasu T, Moriya Y; Colorectal Cancer Study Group of Japan Clinical Oncology Group. Long-term follow-up of the randomized trial of mesorectal excision with or without lateral lymph node dissection in rectal cancer (JCOG0212). *Br J Surg* 2020; **107**: 586-594 [PMID: 32162301 DOI: 10.1002/bjs.11513]

40 **Komori K**, Fujita S, Mizusawa J, Kanemitsu Y, Ito M, Shiomi A, Ohue M, Ota M, Akazai Y, Shiozawa M, Yamaguchi T, Bandou H, Katsumata K, Kinugasa Y, Takii Y, Akasu T, Moriya Y; Colorectal Cancer Study Group of Japan Clinical Oncology Group. Predictive factors of pathological lateral pelvic lymph node metastasis in patients without clinical lateral pelvic lymph node metastasis (clinical stage II/III): The analysis of data from the clinical trial (JCOG0212). *Eur J Surg Oncol* 2019; **45**: 336-340 [PMID: 30477950 DOI: 10.1016/j.ejso.2018.11.016]

41 **Kusters M**, Beets GL, van de Velde CJ, Beets-Tan RG, Marijnen CA, Rutten HJ, Putter H, Moriya Y. A comparison between the treatment of low rectal cancer in Japan and the Netherlands, focusing on the patterns of local recurrence. *Ann Surg* 2009; **249**: 229-235 [PMID: 19212175 DOI: 10.1097/SLA.0b013e318190a664]

42 **Akiyoshi T**, Ueno M, Matsueda K, Konishi T, Fujimoto Y, Nagayama S, Fukunaga Y, Unno T, Kano A, Kuroyanagi H, Oya M, Yamaguchi T, Watanabe T, Muto T. Selective lateral pelvic lymph node dissection in patients with advanced low rectal cancer treated with preoperative chemoradiotherapy based on pretreatment imaging. *Ann Surg Oncol* 2014; **21**: 189-196 [PMID: 23963871 DOI: 10.1245/s10434-013-3216-y]

43 **Ishihara S**, Kawai K, Tanaka T, Kiyomatsu T, Hata K, Nozawa H, Morikawa T, Watanabe T. Oncological Outcomes of Lateral Pelvic Lymph Node Metastasis in Rectal Cancer Treated With Preoperative Chemoradiotherapy. *Dis Colon Rectum* 2017; **60**: 469-476 [PMID: 28383446 DOI: 10.1097/DCR.0000000000000752]

44 **Hazen SJA**, Sluckin TC, Konishi T, Kusters M. Lateral lymph node dissection in rectal cancer: State of the art review. *Eur J Surg Oncol* 2022; **48**: 2315-2322 [PMID: 34802862 DOI: 10.1016/j.ejso.2021.11.003]

45 **Fujita S**, Akasu T, Mizusawa J, Saito N, Kinugasa Y, Kanemitsu Y, Ohue M, Fujii S, Shiozawa M, Yamaguchi T, Moriya Y; Colorectal Cancer Study Group of Japan Clinical Oncology Group. 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**: 616-621 [PMID: 22591948 DOI: 10.1016/S1470-2045(12)70158-4]

46 **Georgiou P**, Tan E, Gouvas N, Antoniou A, Brown G, Nicholls RJ, Tekkis P. Extended lymphadenectomy versus conventional surgery for rectal cancer: a meta-analysis. *Lancet Oncol* 2009; **10**: 1053-1062 [PMID: 19767239 DOI: 10.1016/S1470-2045(09)70224-4]

47 **Ngu JC**, Kuo LJ, Teo NZ, Yusof SB. Teaching pelvic lymph node dissection using origami, planes and boundaries. *Tech Coloproctol* 2020; **24**: 767-769 [PMID: 32185547 DOI: 10.1007/s10151-020-02184-y]

48 **Tang J**, Zhou S, Zhao W, Lou Z, Liang J, Feng B, Yang Y, Wang X, Liu Q; Chinese Lateral Node Collaborative Group. Short- and long-term outcomes of laparoscopic versus open selective lateral pelvic lymph node dissection for locally advanced middle-low rectal cancer: Results of a multicentre lateral node study in China. *Colorectal Dis* 2022; **24**: 1325-1334 [PMID: 35713974 DOI: 10.1111/codi.16223]

49 **Yamaguchi T**, Kinugasa Y, Shiomi A, Tomioka H, Kagawa H. Robotic-assisted laparoscopic versus open lateral lymph node dissection for advanced lower rectal cancer. *Surg Endosc* 2016; **30**: 721-728 [PMID: 26092002 DOI: 10.1007/s00464-015-4266-y]

50 **Yamaguchi T**, Kinugasa Y, Shiomi A, Kagawa H, Yamakawa Y, Furutani A, Manabe S, Yamaoka Y, Hino H. Oncological outcomes of robotic-assisted laparoscopic versus open lateral lymph node dissection for locally advanced low rectal cancer. *Surg Endosc* 2018; **32**: 4498-4505 [PMID: 29721748 DOI: 10.1007/s00464-018-6197-x]

51 **Watanabe J**, Ohya H, Sakai J, Suwa Y, Goto K, Nakagawa K, Ozawa M, Ishibe A, Suwa H, Kunisaki C, Endo I. Long-term outcomes of indocyanine green fluorescence imaging-guided laparoscopic lateral pelvic lymph node dissection for clinical stage II/III middle-lower rectal cancer: a propensity score-matched cohort study. *Tech Coloproctol* 2023; **27**: 759-767 [PMID: 36773172 DOI: 10.1007/s10151-023-02761-x]

52 **Ohya H**, Watanabe J, Suwa H, Suwa Y, Ozawa M, Ishibe A, Kunisaki C, Endo I. Near-Infrared Imaging Using Indocyanine Green for Laparoscopic Lateral Pelvic Lymph Node Dissection for Clinical Stage II/III Middle-Lower Rectal Cancer: A Propensity Score-Matched Cohort Study. *Dis Colon Rectum* 2022; **65**: 885-893 [PMID: 34840301 DOI: 10.1097/DCR.0000000000002156]

53 **Schaap DP**, Boogerd LSF, Konishi T, Cunningham C, Ogura A, Garcia-Aguilar J, Beets GL, Suzuki C, Toda S, Lee IK, Sammour T, Uehara K, Lee P, Tuynman JB, van de Velde CJH, Rutten HJT, Kusters M; Lateral Node Study Consortium. Rectal cancer lateral lymph nodes: multicentre study of the impact of obturator and internal iliac nodes on oncological outcomes. *Br J Surg* 2021; **108**: 205-213 [PMID: 33711144 DOI: 10.1093/bjs/znaa009]

54 **Kim YI**, Jang JK, Park IJ, Park SH, Kim JB, Park JH, Kim TW, Ro JS, Lim SB, Yu CS, Kim JC. Lateral lymph node and its association with distant recurrence in rectal cancer: A clue of systemic disease. *Surg Oncol* 2020; **35**: 174-181 [PMID: 32889250 DOI: 10.1016/j.suronc.2020.08.013]

55 **Lee D**, Matsuda T, Yamashita K, Hasegawa H, Yamamoto M, Kanaji S, Oshikiri T, Nakamura T, Suzuki S, Fukumoto T, Kakeji Y. Significance of Lateral Pelvic Lymph Node Size in Predicting Metastasis and Prognosis in Rectal Cancer. *Anticancer Res* 2019; **39**: 993-998 [PMID: 30711986 DOI: 10.21873/anticanres.13204]

56 **Sapci I**, Delaney CP, Liska D, Amarnath S, Kalady MF, Steele SR, Gorgun E. Oncological Outcomes of Patients with Locally Advanced Rectal Cancer and Lateral Pelvic Lymph Node Involvement. *J Gastrointest Surg* 2019; **23**: 1454-1460 [PMID: 31012043 DOI: 10.1007/s11605-019-04224-x]

57 **Schaap DP**, Ogura A, Nederend J, Maas M, Cnossen JS, Creemers GJ, van Lijnschoten I, Nieuwenhuijzen GAP, Rutten HJT, Kusters M. Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer. *Br J Surg* 2018; **105**: 1844-1852 [PMID: 30079958 DOI: 10.1002/bjs.10949]

58 **Kim MJ**, Hur BY, Lee ES, Park B, Joo J, Kim MJ, Park SC, Baek JY, Chang HJ, Kim DY, Oh JH. Prediction of lateral pelvic lymph node metastasis in patients with locally advanced rectal cancer with preoperative chemoradiotherapy: Focus on MR imaging findings. *PLoS One* 2018; **13**: e0195815 [PMID: 29649321 DOI: 10.1371/journal.pone.0195815]

59 **Kobayashi H**, Kikuchi A, Okazaki S, Ishiguro M, Ishikawa T, Iida S, Uetake H, Sugihara K. Diagnostic performance of multidetector row computed tomography for assessment of lymph node metastasis in patients with distal rectal cancer. *Ann Surg Oncol* 2015; **22**: 203-208 [PMID: 25124470 DOI: 10.1245/s10434-014-3972-3]

60 **Ogawa S**, Hida J, Ike H, Kinugasa T, Ota M, Shinto E, Itabashi M, Kameoka S, Sugihara K. 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**: 1187-1194 [PMID: 26671038 DOI: 10.1245/s10434-015-5021-2]

61 **Ogawa S**, Itabashi M, Hirosawa T, Hashimoto T, Bamba Y, Kameoka S. Lateral pelvic lymph node dissection can be omitted in lower rectal cancer in which the longest lateral pelvic and perirectal lymph node is less than 5 mm on MRI. *J Surg Oncol* 2014; **109**: 227-233 [PMID: 24165955 DOI: 10.1002/jso.23478]

62 **Matsuoka H**, Nakamura A, Masaki T, Sugiyama M, Nitatori T, Ohkura Y, Sakamoto A, Atomi Y. Optimal diagnostic criteria for lateral pelvic lymph node metastasis in rectal carcinoma. *Anticancer Res* 2007; **27**: 3529-3533 [PMID: 17972513]

**Footnotes**

**Conflict-of-interest statement:** All the authors report no relevant conflict of interest for this article

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** August 28, 2023

**First decision:** November 1, 2023

**Article in press:**

**Specialty type:** Surgery

**Country/Territory of origin:** Singapore

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Bustamante-Lopez LA, Brazil; Sano W, Japan **S-Editor:** Liu JH **L-Editor:** A **P-Editor:**

**Table 1 Summary of diagnostic criteria for suspicious lateral pelvic lymph nodes**

|  |  |  |  |
| --- | --- | --- | --- |
| Study | Imaging modality | Nodal size | Nodal features |
| Schaap *et al*[53], 2021 | MRI | Pre-treatment: SAD ≥ 7 mm | - |
| Amano *et al*[23], 2020 | MRI; CT; PET-CT | (MRI or CT) SAD > 6 mm; (PET/CT) increased FDG uptake | - |
| Kim *et al*[54], 2020 | MRI | Pre-treatment: SAD ≥ 7 mm; Post-treatment:  SAD ≥ 4 mm | - |
| Lee *et al*[55], 2019 | CT or MRI | Pre-treatment: SAD ≥ 8 mm | - |
| Sapci *et al*[56], 2019 | MRI | Size > 5 mm | And either heterogeneity or border irregularity |
| Schaap *et al*[57], 2018 | MRI | SAD ≥ 10 mm | - |
| Kim *et al*[58], 2018 | MRI | Pre-treatment: SAD ≥ 5 mm | Signal intensity homo/heterogenous; Margins irregular or well defined; DWI signal intensity high or low; Size reduction rate |
| Akiyoshi *et al*[30], 2015 | MRI | Pre-treatment: SAD ≥ 8 mm | - |
| Kobayashi *et al*[59], 2015 | CT | LAD > 9 mm; SAD > 6 mm | - |
| Ogawa *et al*[60], 2015 | MRI | SAD ≥ 10 mm or ≥ 5 mm (institution-dependent) | Enlarged LPLN on palpation; Enlarged perirectal node or LPLN ≥ 5 mm |
| Ogawa *et al*[61], 2014 | MRI | LAD ≥ 5 mm; LAD < 5 mm | - |
| Shihab *et al*[29], 2011 | MRI | No size criteria | Mixed signal intensity or irregular nodal capsule border |
| Matsuoka *et al*[62], 2007 | MRI | LAD ≥ 10 mm; SAD ≥ 5 mm | Ovoid shape; heterogeneity |

CT: Computed tomography; MRI: Magnetic resonance imaging; LAD: Long axis diameter; SAD: Short axis diameter; LPLN: Lateral pelvic lymph node.