

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2021 October 15; 13(10): 1213-1543



FRONTIER

- 1213** Engineering nanotheranostic strategies for liver cancer

Cao L, Zhu YQ, Wu ZX, Wang GX, Cheng HW

REVIEW

- 1229** Role of autophagy in cholangiocarcinoma: An autophagy-based treatment strategy

Koustas E, Trifylli EM, Sarantis P, Papavassiliou AG, Karamouzis MV

- 1244** Role of autophagy in gastric carcinogenesis

Papaefthymiou A, Christodoulidis G, Koffas A, Doulberis M, Polyzos SA, Manolakis A, Potamianos S, Kapsoritakis A, Kountouras J

- 1263** Liquid biopsy approach to pancreatic cancer

Perales S, Torres C, Jimenez-Luna C, Prados J, Martinez-Galan J, Sanchez-Manas JM, Caba O

- 1288** Molecular testing for colorectal cancer: Clinical applications

Imyanitov E, Kuligina E

- 1302** New frontiers in liver ultrasound: From mono to multi parametricity

Bartolotta TV, Taibbi A, Randazzo A, Gagliardo C

- 1317** Gallbladder cancer: Historical treatment and new management options

Okumura K, Gogna S, Gachabayov M, Felsenreich DM, McGuirk M, Rojas A, Quintero L, Seshadri R, Gu K, Dong XD

- 1336** Review of incidence and outcomes of treatment of cholangiocarcinoma in patients with primary sclerosing cholangitis

Saffioti F, Mavroeidis VK

- 1367** Diverse roles of FOXO family members in gastric cancer

Chen YH, Li CL, Chen WJ, Liu J, Wu HT

MINIREVIEWS

- 1383** Endoscopic radiofrequency ablation for malignant biliary obstruction

Jarosova J, Macinga P, Hujova A, Kral J, Urban O, Spicak J, Hucl T

- 1397** Thermal ablation and immunotherapy for hepatocellular carcinoma: Recent advances and future directions

Bo XW, Sun LP, Yu SY, Xu HX

- 1412** Lateral pelvic lymph nodes for rectal cancer: A review of diagnosis and management

Ogawa S, Itabashi M, Inoue Y, Ohki T, Bamba Y, Koshino K, Nakagawa R, Tani K, Aihara H, Kondo H, Yamaguchi S, Yamamoto M

- 1425** Proliferating cell nuclear antigen clamp associated factor, a potential proto-oncogene with increased expression in malignant gastrointestinal tumors
Liu LJ, Liao JM, Zhu F
- 1440** Nutritional therapy for hepatocellular carcinoma
Ruiz-Margáin A, Román-Calleja BM, Moreno-Guillén P, González-Regueiro JA, Kúsulas-Delint D, Campos-Murguía A, Flores-García NC, Macías-Rodríguez RU
- 1453** Radiotherapy for gastric mucosa-associated lymphoid tissue lymphoma
Quéro L, Labidi M, Bollet M, Bommier C, Guillermin S, Hennequin C, Thieblemont C
- 1466** Endoscopic papillectomy for ampullary adenomatous lesions: A literature review
Li SL, Li W, Yin J, Wang ZK
- 1475** Endoscopic ultrasound assessment and tissue acquisition of mediastinal and abdominal lymph nodes
Tamanini G, Cominardi A, Brighi N, Fusaroli P, Lisotti A

ORIGINAL ARTICLE

Basic Study

- 1492** Direct interaction between Rab5a and Rab4a enhanced epidermal growth factor-stimulated proliferation of gastric cancer cells
Cao GJ, Wang D, Zeng ZP, Wang GX, Hu CJ, Xing ZF
- 1506** Combination of neutrophil gelatinase-associated lipocalin and matrix metalloproteinase-9 are biomarkers for the detection of colon tubular adenocarcinoma
Yuan JH, Xie LS, Zhu YH, Wang XH, Zhang YJ, Wang XJ
- 1518** Survival effect of probiotics in a rat model of colorectal cancer treated with capecitabine
Gigola G, Carriere P, Novoa Díaz MB, Perdigon G, Zwenger AO, Gentili C

Prospective Study

- 1532** Efficacy and toxicity of capecitabine combined with intensity-modulated radiotherapy after D1/D2 lymph node dissection in patients with gastric cancer
Wang X, Wang WH, Wang SL, Song YW, Liu YP, Tang Y, Li N, Liu WY, Fang H, Li YX, Zhao DB, Chi Y, Yang L, Jin J

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Guido Giordano, MD, Research Assistant Professor, Department of Medical and Surgical Sciences; Unit of Medical Oncology and Biomolecular Therapy, University of Foggia, Policlinico Riuniti, Foggia 71122, Italy. giordano.guido81@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (WJGO, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

INDEXING/ABSTRACTING

The WJGO is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJGO as 3.393; IF without journal self cites: 3.333; 5-year IF: 3.519; Journal Citation Indicator: 0.5; Ranking: 163 among 242 journals in oncology; Quartile category: Q3; Ranking: 60 among 92 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO's CiteScore for 2020 is 3.3 and Scopus CiteScore rank 2020: Gastroenterology is 70/136.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Ya-Juan Ma*.

NAME OF JOURNAL

World Journal of Gastrointestinal Oncology

ISSN

ISSN 1948-5204 (online)

LAUNCH DATE

February 15, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Rosa M Jimenez Rodriguez, Pashtoon Kasi, Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

PUBLICATION DATE

October 15, 2021

COPYRIGHT

© 2021 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Lateral pelvic lymph nodes for rectal cancer: A review of diagnosis and management

Shimpei Ogawa, Michio Itabashi, Yuji Inoue, Takeshi Ohki, Yoshiko Bamba, Kurodo Koshino, Ryosuke Nakagawa, Kimitaka Tani, Hisako Aihara, Hiroka Kondo, Shigeki Yamaguchi, Masakazu Yamamoto

ORCID number: Shimpei Ogawa 0000-0003-4196-7261; Michio Itabashi 0000-0003-2664-1984; Yuji Inoue 0000-0002-1383-8596; Takeshi Ohki 0000-0002-6328-0754; Yoshiko Bamba 0000-0002-7139-8576; Kurodo Koshino 0000-0001-9027-730X; Ryosuke Nakagawa 0000-0001-6428-1209; Kimitaka Tani 0000-0001-8078-1369; Hisako Aihara 0000-0003-2214-3320; Hiroka Kondo 0000-0003-1416-4383; Shigeki Yamaguchi 0000-0003-3850-2818; Masakazu Yamamoto 0000-0001-6027-620X.

Author contributions: Ogawa S, Itabashi M, Inoue Y, Ohki T, Bamba Y, Koshino K, Nakagawa R, Tani K, Aihara H, Kondo H, Yamaguchi S and Yamamoto M conceptualized and designed the study; Ogawa S performed the data analysis and interpretation; Ogawa S and Itabashi M revised the manuscript for important intellectual content; Ogawa S, Itabashi M and Yamamoto M provided the final approval for the manuscript to be published.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

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

Shimpei Ogawa, Michio Itabashi, Yuji Inoue, Takeshi Ohki, Yoshiko Bamba, Kurodo Koshino, Ryosuke Nakagawa, Kimitaka Tani, Hisako Aihara, Hiroka Kondo, Shigeki Yamaguchi, Masakazu Yamamoto, Department of Surgery, Institute of Gastroenterology, Tokyo Women's Medical University, Tokyo 162-8666, Japan

Corresponding author: Shimpei Ogawa, MD, PhD, Associate Professor, Department of Surgery, Institute of Gastroenterology, Tokyo Women's Medical University, 8-1, Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan. ogawa.shimpei@twmu.ac.jp

Abstract

The current status and future prospects for diagnosis and treatment of lateral pelvic lymph node (LPLN) metastasis of rectal cancer are described in this review. Magnetic resonance imaging (MRI) is recommended for the diagnosis of LPLN metastasis. A LPLN-positive status on MRI is a strong risk factor for metastasis, and evaluation by MRI is important for deciding treatment strategy. LPLN dissection (LPLD) has an advantage of reducing recurrence in the lateral pelvis but also has a disadvantage of complications; therefore, LPLD may not be appropriate for cases that are less likely to have LPLN metastasis. Radiation therapy (RT) and chemoradiation therapy (CRT) have limited effects in cases with suspected LPLN metastasis, but a combination of preoperative CRT and LPLD may improve the treatment outcome. Thus, RT and CRT plus selective LPLD may be a rational strategy to omit unnecessary LPLD and produce a favorable treatment outcome.

Key Words: Diagnosis; Treatment; Rectal cancer; Lateral pelvic lymph node metastasis; Lateral pelvic lymph node dissection; Radiotherapy

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Diagnosis of lateral pelvic lymph node (LPLN) metastasis of rectal cancer is mainly made using magnetic resonance imaging (MRI). LPLN-positive status on MRI is a strong risk factor for metastasis, and evaluation by MRI is important for deciding treatment strategy. LPLN dissection (LPLD) reduces recurrence in the lateral pelvis but also has complications and may not be appropriate for cases predicted to not have

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: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: Japan

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 21, 2021

Peer-review started: February 21, 2021

First decision: May 8, 2021

Revised: May 21, 2021

Accepted: August 24, 2021

Article in press: August 24, 2021

Published online: October 15, 2021

P-Reviewer: Fernandez Escamez CS

S-Editor: Ma YJ

L-Editor: A

P-Editor: Guo X



LPLN metastasis. Preoperative radiation therapy (RT) or chemoradiation therapy (CRT) can improve the treatment outcome. Thus, RT and CRT plus selective LPLD may produce favorable treatment outcomes.

Citation: Ogawa S, Itabashi M, Inoue Y, Ohki T, Bamba Y, Koshino K, Nakagawa R, Tani K, Aihara H, Kondo H, Yamaguchi S, Yamamoto M. Lateral pelvic lymph nodes for rectal cancer: A review of diagnosis and management. *World J Gastrointest Oncol* 2021; 13(10): 1412-1424

URL: <https://www.wjgnet.com/1948-5204/full/v13/i10/1412.htm>

DOI: <https://dx.doi.org/10.4251/wjgo.v13.i10.1412>

INTRODUCTION

Colorectal cancer (CRC) is the third most frequently diagnosed cancer worldwide, with an estimated 1.9 million new cases reported annually[1]. Moreover, CRC accounts for 9.4% of all cancer deaths, and about one-third of CRC cases are represented by rectal cancer. Lymph node (LN) metastasis is a risk factor for local recurrence and a poor prognostic factor in rectal cancer, and the treatment strategy is important. Rectal lymph flows upward, laterally and downward, and LN metastasis mainly advances along the mesorectal nodal chain along the inferior mesenteric artery nodes[2-5]. Lower rectal cancer on the anal side from the peritoneal reflection also advances to LNs of the extramesorectal lateral pelvis. The frequency of lateral pelvic lymph node (LPLN) metastasis of lower rectal cancer is 11.3%-22.4%, and the outcome of cases with LPLN metastasis is poor[6-13]. Regarding treatment outcomes, the survival rates of cases with internal iliac LN metastasis and more distant LPLN metastasis are comparable to those of the tumor-node-metastasis (TNM) classifications N2a and N2b, respectively[10].

In lower rectal cancer, local recurrence occurs as frequently as liver metastasis and lung metastasis, and reportedly in 4%-10% of rectal cancer cases treated with total mesorectal excision (TME) alone[14,15]. Of local recurrence cases, recurrence in the lateral pelvis is accompanied by serious complications, the possibility of salvage is low, and many patients do not survive, making this a significant clinical problem[16]. Moreover, $\geq 40\%$ of LPLN metastasis cases with local recurrence do not have distant metastasis, which indicates the importance of local control[17]. Therefore, LPLN metastasis is closely linked to the treatment outcome of lower rectal cancer and control of LPLN metastasis may be key to improvement of outcomes. In this review, the current status and future prospects of diagnosis and treatment of LPLN metastasis of rectal cancer are discussed.

DIAGNOSIS OF LN METASTASIS OF RECTAL CANCER

LN metastasis of rectal cancer can be evaluated by endoscopic ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and [^{18}F]fluorodeoxyglucose-positron emission tomography (FDG-PET)[18]. Of these imaging modalities, MRI has superior contrast resolution of soft tissue and is an excellent method with multiplanar imaging capacity that is useful for the N staging of rectal cancer[19]. In the European Society for Medical Oncology (ESMO) guidelines, endorectal ultrasound is the recommendation for invasion depth evaluation in T1 cases, whereas MRI is recommended for evaluation of T2 or deeper invasion and LN metastasis because it can evaluate a wide range inside and outside the mesorectum[18,20].

Diagnosis of LPLN metastasis by MRI

Diagnosis of LN metastasis of rectal cancer has been widely investigated in the perirectal lymph nodes (PRLNs), whereas fewer studies have investigated LPLNs[21]. The cut-off for LPLN size varies from 4 mm to 12 mm. Similar to those for PRLNs, various morphological criteria have also been described, including irregular border, mixed signal intensity, speculated appearance, indistinct border, and mottled heterogeneous appearance[22-34]. In a comparison of area under the curve-based diagnoses using 5-mm and 10-mm cut-offs for the short axis, we found values of 0.7418 on the

right and 0.7593 on the left at 5-mm, and of 0.6326 on the right and 0.6559 on the left at 10-mm[35]. The 5-mm values were significantly higher and indicated excellent diagnostic ability using a 5-mm short axis cut-off (Table 1).

Diagnosis of LPLN metastasis based on size criteria

Results supporting the validity of size-based LPLN diagnosis have been reported. Ueno *et al*[11] divided the lateral region of excised specimens into six areas and compared the size of metastasis-positive and -negative LNs in each area, yielding the observation that the size of metastasis-positive LNs was significantly larger in all areas. Akasu *et al*[27] reported a relationship between LN size on MRI and histological metastasis for PRLNs and LPLNs. In PRLNs, the overlap of metastasis-positive and -negative LNs was large, as reported by Brown *et al*[36], but the overlap was small for LPLNs and very small or non-existent LNs that were visualized on imaging in most metastasis-negative cases; thus, the size criterion was concluded to work well.

LPLN-positive status on MRI as a risk factor for LPLN metastasis

Female sex, lower rectum involvement, histopathological grade other than well or moderately differentiated adenocarcinoma, lymphatic invasion, venous invasion, wall depth of invasion \geq pT3, and PRLN metastasis have been reported as risk factors of LPLN metastasis of rectal cancer[6-10,37-39]. LPLN-positive status on imaging has also been identified as a risk factor. Fujita *et al*[9] defined cases with LPLNs of \geq 5 mm on CT as LPLN-positive, and found the LPLN-positive status to be an independent risk factor for LPLN metastasis, with an odds ratio (OR) of 28.00, which was higher than that of other risk factors. We also found LPLN-positive status on MRI to be an independent risk factor, together with age ($<$ 64 years), histopathological grade (G3 + G4), M1, and pPRLN(+) status, with ORs for right and left LPLNs of 10.73 and 24.53, respectively[40]. These values were higher than those for the other risk factors, showing the importance of a LPLN-positive status on MRI.

Current diagnosis of LPLN metastasis

Size-based diagnosis of LN metastasis of rectal cancer by MRI is simple and has only small inter-observer differences compared with those in morphology-based diagnosis, suggesting that size-based diagnosis is the most reliable, clinically[27]. Kim *et al*[17] also stated that LN size is the most reliable parameter for diagnosis of LN metastasis by MRI and that 5 mm is the most common criterion. In a meta-analysis of preoperative evaluation of rectal cancer by MRI, diagnosis of LN metastasis was evaluated as poor based on the diagnostic odds ratio (*i.e.*, "DOA") compared with those of the circumferential resection margin (CRM) and T category[21]. The diagnostic ability of LPLN by MRI had a pooled sensitivity, specificity, and DOA of 0.72, 0.80, and 10.2, respectively, in a meta-analysis[41], showing the need for further studies to improve this performance.

New diagnostic method for LN metastasis of rectal cancer

Diffusion-weighted MRI, Gadofosveset-enhanced MRI, and LN-specific contrast medium ultrasmall superparamagnetic iron oxide contrast agent (*i.e.* 'USPIO')-enhanced MRI have been examined for improvement of diagnosis of LN metastasis of rectal cancer[42-48]. Using differences in enhancement patterns of Gadofosveset-enhanced MRI, the favorable results of negative predictive values of $>$ 95% per lesion and $>$ 85% per patient have been reported[42]. Regarding USPIO-enhanced MRI, USPIO is not approved for clinical use in Japan and its routine use in medical practice is not approved in Western countries, although favorable results (sensitivity of 93%, specificity of 96%) have been reported[43-45]. FDG-PET in combination with CT and MRI has been examined in post-CRT cases, with the cut-off for each method being determined from a receiver operating characteristic curve. Diagnosis using combined cut-offs of 12 mm on CT and MRI and SUVmax of 1.6 on FDG-PET give accuracy of 92.9%, sensitivity of 88.2%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 84.6%[46].

TREATMENT STRATEGIES FOR RECTAL CANCER LPLN METASTASIS IN GUIDELINES

Treatment strategies for LPLN metastasis of rectal cancer differ between Eastern countries, especially Japan, and Western countries. In Japan, LPLN metastasis, which

Table 1 Studies of magnetic resonance imaging diagnosis and criteria for lateral pelvic lymph node metastasis

Ref.	Patients	Accuracy	Sensitivity	Specificity	PPV	NPV	Criteria
Kim <i>et al</i> [22], 1999	8				12.5%		> 1.2 cm
Kim <i>et al</i> [23], 2000	14				29%		> 10 mm
Arii <i>et al</i> [24], 2006	53	83%	56%	97%	91%	81%	> 7 mm Round shape
Matsuoka <i>et al</i> [25], 2007	51	78%	67%	83%			≥ 5 mm (short-axis) Ovoid shape
Min <i>et al</i> [26], 2009	66				86.4%		> 1.0 cm, > 0.5 cm (short-axis) Spiculated or indistinct borders, mottled heterogenic pattern
Akasu <i>et al</i> [27], 2009	104	87%	87%	87%	52%	97%	≥ 4 mm (short-axis)
Lim <i>et al</i> [28], 2013	67				39.0%		≥ 5 mm (short-axis) Spiculated or indistinct border, mottled heterogenic pattern
Akiyoshi <i>et al</i> [29], 2015	77		68%	85%			≥ 8 mm (short-axis)
Ishibe <i>et al</i> [30], 2016	84	88.1%	43.8%	98.5%	87.5%	88.1	≥ 10 mm (short-axis)
Lee <i>et al</i> [33], 2019	37		85.7%	84.0%	12.5%	99.5%	≥ 7 mm (short-axis)
Ogawa <i>et al</i> [35], 2016	268 (right)	77.6%	68.6%	79.7%	44.3%	91.5%	≥ 5 mm (short-axis)
	280 (left)	79.3%	70.8%	81.0%	43.6%	93.1%	

NPV: Negative predictive value; PPV: Positive predictive value.

is defined as progression beyond the mesorectum, is considered controllable by surgical LPLN dissection (LPLD), and TME + LPLD is the standard surgical procedure for advanced lower rectal cancer[49-51]. LPLNs are handled as regional LNs and the Japanese treatment guidelines for CRC recommend prophylactic dissection for T3 or deeper lower rectal cancer, even in cases without suspected LPLN metastasis[51]. In contrast, in Western countries, LPLN metastasis is handled as a systemic disease because distant metastasis is common and the outcome is poor[52,53].

In the American Joint Committee on Cancer (*i.e.*, "AJCC") Cancer Staging Manual, for the lateral pelvic regions, LNs in the internal iliac region, but not those in the obturator, external iliac and common iliac regions, are classified as regional LNs, and metastasis to the lateral pelvic regions, except of the internal iliac region, is handled as distant metastasis[54]. In Western countries, a combination of TME with radiation therapy (RT) and chemoradiation therapy (CRT) is the standard treatment for advanced lower rectal cancer because preoperative RT and CRT exhibit a partial local control effect. The combination of preoperative RT or CRT has been reported to reduce local recurrence to ≤ 10%[55].

The National Comprehensive Cancer Network (*i.e.*, "NCCN") guidelines recommend TME after CRT with concomitant fluorouracil for cStage II-III rectal cancer [56]. Induction chemotherapy before CRT is also recommended as a standard treatment. There is no specific description for LPLD, but extended dissection of LNs located outside the resection region, to which LPLNs correspond, is indicated for resectable LNs with suspected metastasis, whereas prophylactic dissection is not particularly recommended for LNs without suspected metastasis.

In the ESMO guidelines, the recurrence risk is classified into "early", "intermediate", "bad", and "advanced" based on the distance of the tumor from the anal verge, the T stage and N stage, while use of TME alone, preoperative RT, and preoperative CRT is recommended depending on the risk[18]. There is no description concerning prophylactic LPLD, and when LPLN metastasis is suspected, the case is classified as "advanced", with preoperative CRT followed by surgery (TME and more extensive surgery if indicated by tumor overgrowth) or preoperative short-course preoperative RT (5 × 5 Gy) plus the folinic acid + fluorouracil + oxaliplatin (*i.e.*, "FOLFOX") regimen and a delay of surgery are described as treatment methods. The ESMO guidelines also do not particularly recommend prophylactic dissection for LPLNs without suspected metastasis, similar to the NCCN guidelines, and LPLD is

not routinely performed in Western countries.

LPLD and CRT for cLPLN(-) cases

Many studies on the treatment outcomes of LPLD have been reported, mainly from Japan[7,13,57,58]. Kanemitsu *et al*[13] determined the 5-year overall survival (OS) rates in LPLN metastasis(+) cases treated with LPLD at two high-volume centers in Japan as 53.1% and 45.2%, respectively, compared to those in LPLN metastasis(-) cases, which were 81.7% and 81.0%, respectively. The local recurrence risk ratio of unilateral to bilateral LPLD cases was 2.0, indicating the necessity of bilateral dissection. In a comparison of cases treated with and without LPLD in a matched cohort study, the 5-year OS rates were 68.9% and 62.0%, respectively, with a significantly higher OS in cases treated with LPLD[58].

The results of the JCOG0212 randomized controlled trial have provided insights into the outcomes of prophylactic LPLD in cLPLN(-) cases without suspected metastasis[57]. This trial examined TME alone (designated as the ME group) compared to TME + LPLD (designated as the LPLD group) as standard treatment. The primary endpoint of 5-year relapse-free survival (RFS) was 73.4% in the LPLD group and 73.3% in the ME group, which did not demonstrate non-inferiority of TME alone; moreover, the Kaplan-Meier curve for RFS was consistent, showing no superiority of LPLD. The secondary endpoint of 5-year OS was 92.6% in the LPLD group and 90.2% in the ME group, again showing no significant difference. The 5-year local recurrence-free rates were 87.7% in the LPLD group and 82.4% in the ME group, with no significant difference, but the local recurrence rate was significantly lower in the LPLD group [26 cases (7.4%) *vs* 44 cases (12.6%), $P = 0.024$]. Local recurrence was in the lateral pelvis in 4 and 23 cases in the respective groups. Thus, recurrence in the lateral pelvis occurred in fewer cases in the LPLD group, indicating that LPLD is effective for reduction of recurrence in this region.

One reason for non-performance of LPLD in Western countries is that superiority of the treatment effect of LPLD compared to RT and CRT has not been demonstrated [52]. Kusters *et al*[59] adjusted patient background factors and compared treatment outcomes in a Japanese group (designated as the “NCCH” group) treated with TME + LPLD and groups treated with TME alone and RT + TME in a Dutch trial. The 5-year local recurrence rate was 6.9% in the Japanese NCCH group, 5.8% in the Dutch RT + TME group, and 12.1% in the Dutch TME-alone group. Thus, this rate was lower with TME + LPLD and TME + RT than with TME alone, and both LPLD and RT indicated a partial local control effect compared with TME alone. There was no difference between the effects of TME + LPLD and TME + RT.

Nagawa *et al*[60] performed 50-Gy preoperative RT in 45 patients with lower rectal cancer without LPLN enlargement in cases treated with TME alone and TME + LPLD. There was no difference in the OS and local recurrence rates between the two groups, and accordingly it was concluded that LPLD is unnecessary for lower rectal cancer without LPLN enlargement before treatment if preoperative RT is performed. In addition, Watanabe *et al*[61] also found no difference in the survival rate between RT-treated non-LPLD cases and LPLD-treated non-RT cases. In these studies, even though LPLD was added before treatment, if LPLN metastasis was not suspected before treatment, the oncological effect was small and the tumor could be controlled by preoperative RT. This suggests that a favorable outcome may be acquired even with TME alone if preoperative RT is performed.

The other reason for not performing LPLD in Western countries is the complications associated with LPLD[52]. Intraoperative complications of a long operative time and large-volume blood loss, and postoperative complications such as urinary and sexual dysfunction have been reported in LPLD-treated cases. Similarly, in the JCOG0212 study, the operative time was significantly longer and blood-volume loss was larger in the LPLD group, and the incidence of grade 3 or more severe complications was 22% in the LPLD group but only 16% in the ME group treated without LPLD[62]. In a recent meta-analysis, only Gao *et al*[63] reported a significantly lower 5-year local recurrence rate after LPLD than that in cases without LPLD treatment. In most reports, there was no difference in OS, DFS, or local recurrence (Tables 2 and 3)[63-69]. Postoperative urinary and sexual dysfunction was common, the operative time was long, and blood-volume loss was large in LPLD cases, but there are also serious complications of RT and CRT. These include dysuria, dyschezia, sexual dysfunction and secondary cancer as late complications and perineal wound complication of abdominoperineal resection and an influence on defecation function in cases treated with sphincter-preserving surgery[70-72].

Table 2 Variables in treatment of lateral pelvic lymph node dissection in recent meta-analyses and systematic reviews

Ref.	Study (RCT)	Treatment	Patients	CRT or RT	OS	DFS	TR	LR	LLR
Gao <i>et al</i> [63], 2020	12 (6)	TME + LPLD	1952	359	5-yr HR 0.93, 95%CI: 0.71-1.22, <i>P</i> = 0.62	5-yr HR 0.99, 95%CI: 0.74-1.34, <i>P</i> = 0.96	5-yr RR 0.98, 95%CI: 0.81-1.18, <i>P</i> = 0.83	5-yr RR 0.71, 95%CI: 0.56-0.89, <i>P</i> = 0.003	5-yr RR 0.49, 95%CI: 0.18-1.28, <i>P</i> = 0.14
		TME	2506	1009					
Wang <i>et al</i> [64], 2020	16 (4)	TME + LPLD	2984		HR 1.11, 95%CI: 0.77-1.61, <i>P</i> = 0.57	HR 1.05, 95%CI: 0.85-1.30, <i>P</i> = 0.64		OR 0.93, 95%CI: 0.56-1.54, <i>P</i> = 0.78	
		TME	3397						
Ma <i>et al</i> [65], 2020	26 (5)	TME + LPLD	3171	417	5-yr HR 1.14, 95%CI: 0.85-1.54	5-yr HR 1.07, 95%CI: 0.89-1.28, <i>P</i> = 0.496	OR 1.00, 95%CI: 0.80-1.24	OR 0.90, 95%CI: 0.76-1.06, <i>P</i> = 0.208	
		TME	3694	1102					
Emile <i>et al</i> [66], 2020	29 (5)	TME + LPLD	4194	551	HR 1.056, 95%CI: 0.98-1.13, <i>P</i> = 0.13	HR 1.02, 95%CI: 0.97-1.07, <i>P</i> = 0.37		HR 0.96, 95%CI: 0.75-1.25, <i>P</i> = 0.79	
		TME	6452	1467					
Hajibandeh <i>et al</i> [67], 2020	18 (2)	TME + LPLD	2762	321	5-yr OR 1.01, 95%CI: 0.78-1.30, <i>P</i> = 0.94	5-yr OR 1.07, 95%CI: 0.86-1.32, <i>P</i> = 0.54			
		TME	3371	735			OR 0.97, 95%CI: 0.72-1.29, <i>P</i> = 0.82	OR 1.01, 95%CI: 0.72-1.42, <i>P</i> = 0.97	
Law <i>et al</i> [68], 2020	6 (0)	CRT + TME + LPLD	268	268		5-yr OR 0.70, 95%CI: 0.20-2.39, <i>P</i> = 0.57		5-yr OR 0.42, 95%CI: 0.14-1.24, <i>P</i> = 0.12	
		CRT + TME	1210	1210					
Yang <i>et al</i> [69], 2020	8 (1)	CRT + TME + LPLD	435	435					
		CRT + TME	1461	1461	HR 0.78, 95%CI: 0.32-1.88, <i>P</i> = 0.58	HR 0.94, 95%CI: 0.62-1.43, <i>P</i> = 0.77		OR 0.82, 95%CI: 0.27-2.46, <i>P</i> = 0.72	OR 2.99, 95%CI: 1.20-7.44, <i>P</i> = 0.02

CI: Confidence interval; CRT: Chemoradiation therapy; DFS: Disease-free survival; HR: Hazard ratio; LLR: Local lateral recurrence; LPLD: Lateral pelvic lymph node dissection; LR: Local recurrence; OR: Odds ratio; OS: Overall survival; RCT: Randomized controlled trial; RR: Risk ratio; RT: Radiation therapy; TME: Total mesorectal excision; TR: Total recurrence.

LPLD and CRT for cLPLN(+) cases

Difficulty with control of LPLN metastasis by RT or CRT alone has been reported. In cLPLN(+) cases with suspected LPLN metastasis, Kim *et al*[17] found local recurrence in 29 (7.9%) of 366 cases treated with TME alone without LPLD after preoperative CRT. Recurrence in the lateral pelvis was found in 24 (82.7%) of these cases and the local recurrence rates according to pretreatment LPLN size were 2.3%, 12.5% and 68.8% in cases with sizes < 5 mm, 5-10 mm and > 10 mm, showing that this rate was high in cases with LPLN enlargement. In 66 cases with LPLNs with a short axis of > 5 mm on MRI after CRT, Oh *et al*[73] found metastasis in LPLD in 22 (33.3%). Recurrence in the lateral pelvis reportedly occurs in 30%-60% of cases with post-treatment LPLNs of size ≥ 10 mm[74,75]. These reports show that control of LPLN metastasis by RT and CRT is difficult in cases with LPLN enlargement that is suspected to be due to metastasis. In contrast, LPLD has been found to be effective for CRT cases with LPLN enlargement and suspected metastasis[39,76-78].

In 127 CRT-treated cases, Akiyoshi *et al*[76] performed TME alone in 89 cases without suspected LPLN metastasis before treatment (the TME group) and TME + LPLD in 38 suspected cases (LPLD group). LPLN metastasis was found in 25 (65.8%) cases in the LPLD group, but local recurrence was noted in only 7 (7.9%) cases in the TME group and 1 (2.6%) case in the LPLD group. Lateral pelvic recurrence was found in only 3 cases (3.4%) in the TME group and none in the LPLD group. The 3-year RFS was 74.6% in the TME group and 83.8% in the LPLD group, with no significant

Table 3 Variables in complications of lateral pelvic lymph node dissection in recent meta-analyses and systematic reviews

Ref.	Study (RCT)	Treatment	Patients	CRT or RT	Operation time	Blood loss	Complications	Urinary dysfunction	Sexual dysfunction
Gao <i>et al</i> [63], 2020	12 (6)	TME + LPLD	1952	359	WMD 97.03 min, 95%CI: 75.35-118.72, $P < 0.001$	WMD 303.20 mL, 95%CI: 156.82-449.58, $P < 0.001$	RR 1.35, 95%CI: 1.05-1.74, $P = 0.02$	Pooled RR 1.44, 95%CI: 0.63-3.28, $P = 0.38$	Pooled RR 1.41, 95%CI: 0.87-2.31, $P = 0.17$
		TME	2506	1009					
Wang <i>et al</i> [64], 2020	16 (4)	TME + LPLD	2984				OR 1.48, 95%CI: 1.07-2.03, $P = 0.02$	OR 1.60, 95%CI: 0.66-3.87, $P = 0.3$	
		TME	3397						
Ma <i>et al</i> [65], 2020	26 (5)	TME + LPLD	417	417	WMD 92.50 min, 95%CI: 75.63-109.37	WMD 283.89 mL, 95%CI: 183.00-384.79	OR 1.30, 95%CI: 1.04-1.63	OR 2.14, 95%CI: 1.21-3.79, $P = 0.009$	OR 4.19, 95%CI: 1.55-11.33, $P = 0.005$
		TME	1102	1102					
Emile <i>et al</i> [66], 2020	29 (5)	TME + LPLD	4194	551	360 min (median), range 310-540, $P = 0.02$	582 mL (median), $P = 0.4$	OR 1.48, 95%CI: 1.18-1.87, $P < 0.001$	OR 2.1, 95%CI: 1.21-3.67, $P = 0.008$	OR 1.62, 95%CI: 0.94-2.79, $P = 0.08$
		TME	6452	1467	294.7 min (median) range 206-480	337 mL (median)			
Hajibandeh <i>et al</i> [67], 2020	18 (2)	TME + LPLD	2762	321	MD 116.02, 95%CI: 89.20-142.83, $P < 0.00001$		OS 1.59, 95%CI: 1.14-2.24, $P = 0.007$	OR 6.66, 95%CI: 3.31-13.39, $P < 0.00001$	OR 9.67, 95%CI: 2.38-39.26, $P = 0.002$
		TME	3371	735					
Yang <i>et al</i> [69], 2020	8 (1)	CRT + TME + LPLD	435	435					
		CRT + TME	1461	1461	MD -138.63 min, 95%CI: -219.66--57.60, $P < 0.01$	MD -226.24 mL, 95%CI: -505.76-53.27, $P = 0.11$		OR 0.20, 95%CI: 0.08-0.48, $P < 0.01$	

CI: Confidence interval; CRT: Chemoradiation therapy; LPLD: Lateral pelvic lymph node dissection; MD: Mean difference; OR: Odds ratio; RCT: Randomized controlled trial; RR: Risk ratio; RT: Radiation therapy; TME: Total mesorectal excision; WMD: Weighted mean difference.

difference. The 3-year RFS was 77.4% and the 3-year local recurrence rate was 5.8% in the entire cohort, showing favorable results.

Akiyoshi *et al*[77] also found LPLN metastasis in 57 (26.9%) of 212 cases with LPLN enlargement and LPLD treatment, in a study of 613 cases. Recurrence in the lateral pelvis occurred in 20 (76.9%) of 26 cases with local recurrence (5 with unilateral dissection, 15 without LPLD) and the 3-year DFS was 70% in LPLN metastasis(+) cases, which was significantly poorer than that of 88% in ypN0 cases but significantly favorable compared with that of 48% in ypN2 LPLN metastasis(-) cases. The 3-year cumulative local recurrence rate in LPLN metastasis(+) cases was 3.6%, which was significantly lower than that of 17% in ypN2 LPLN metastasis(-) cases and not significantly different from that of 8.0% in ypN1 LPLN metastasis(-) cases.

Ogura *et al*[78] found LPLN enlargement in 327 patients who underwent laparoscopic surgery. Metastasis was present in 26 (24.3%) of 107 cases treated with TME + LPLD. The operative time was significantly longer and blood-volume loss was larger in LPLD compared to non-LPLD cases but there was no significant difference in the incidence of major complications. The 3-year RFS rates were 84.7% and 82.0% in the LPLD and non-LPLD groups, respectively, and the local recurrence rate was 3.2% in the LPLD group and 5.2% in the TME group, with no significant differences between.

A recent meta-analysis similarly found no difference in OS between TME + CRT and TME + CRT + LPLD (Table 2)[68,69]. Yang *et al*[69] found no difference in overall local recurrence in cases with suspected LPLN metastasis but the incidence of local recurrence in the lateral pelvic region was significantly lower in the TME + CRT + LPLD group than in the TME + CRT group.

Treatment strategy for LPLN in rectal cancer cases

The main advantage of LPLD is its ability to reduce the rate of lateral pelvic recurrence, but disadvantages such as a longer operative time as well as increased blood-volume loss and complications suggest that LPLD is not likely to be needed for cases that are unlikely to have LPLN metastasis, provided that the diagnosis is accurate. We have suggested possible omission of LPLD in LPLN metastasis-negative cases with a long LPLN axis of ≤ 5 mm on MRI[79]. A sub-analysis by stage in the JCOG0212 study showed improvement of RFS in clinical stage III in the LPLD group, based on which LPLD is recommended for stage III cases and can be omitted for stage II cases without improvement[80].

The JCOG0212 study also demonstrated a reduction effect of LPLD on recurrence in the lateral pelvis but not on local recurrence in the central region and anastomotic part of the pelvis[57]. A high local recurrence rate has been found in cases with a short CRM on MRI, and there is evidence to suggest that RT and CRT aimed at shrinking the tumor and securing the CRM may be effective in these cases[81,82]. In Japan, TME + LPLD is the standard treatment for advanced lower rectal cancer, but the latest guidelines recommend preoperative CRT for rectal cancer with a high local recurrence risk, although the recommendation is not strong[51]. Cases in which a sufficient CRM cannot be secured may correspond to this high-risk rectal cancer and preoperative CRT may be considered for these cases.

RT and CRT have not been performed in many previous studies on LPLN and it is thought that the outcome is poor and the local recurrence rate is high in LPLN metastasis cases[7,10,13,83]. No prospective comparative study on LPLD following RT and CRT has been performed in cases with suspected LPLN metastasis. As described above, preoperative RT and CRT cannot reduce LPLN metastasis and their effects are limited, but for cases with suspected LPLN metastasis, a combination of preoperative CRT and LPLD may improve outcomes[76,78,84-91]. Thus, preoperative RT and CRT + selective LPLD may be a rational strategy for omitting unnecessary LPLD while acquiring a favorable treatment outcome.

CONCLUSION

In Western countries, LPLN metastasis is handled as a systemic disease, due to concerns about the treatment effect and the many complications of LPLD. However, the efficacies of RT boost (strengthening) and a combination of CRT and LPLD for LPLN metastasis have recently been reported in Western countries[85,92-95]. The accuracy of diagnostic imaging largely depends on the diagnostic equipment and may be increased by modification of this equipment and development of contrast media. This suggests that the significance of prophylactic LPLD will further decrease for LPLNs that are less likely to be metastasized. RT and CRT are rational methods that can omit unnecessary LPLD while giving a favorable treatment outcome. Current multidisciplinary treatment of rectal cancer, in addition to RT and CRT, which are local treatments, is progressing toward a strategy of use of systemic chemotherapy aimed at controlling distant metastasis and improving survival. Both multidisciplinary treatment and LPLD are established and further improvement of treatment outcomes can be expected by utilizing the advantages of these methods with optimum indications.

REFERENCES

- 1 **Sung H**, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]
- 2 **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]
- 3 **Blair JB**, Holyoke EA, Best RR. A note on the lymphatics of the middle and lower rectum and anus. *Anat Rec* 1950; **108**: 635-644 [PMID: 14799884 DOI: 10.1002/ar.1091080402]
- 4 **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]
- 5 **Koh DM**, Brown G, Husband JE. Nodal staging in rectal cancer. *Abdom Imaging* 2006; **31**: 652-659 [PMID: 16897279 DOI: 10.1007/s00261-006-9021-3]
- 6 **Ueno M**, Oya M, Azekura K, Yamaguchi T, Muto T. Incidence and prognostic significance of lateral

- lymph node metastasis in patients with advanced low rectal cancer. *Br J Surg* 2005; **92**: 756-763 [PMID: 15838895 DOI: 10.1002/bjs.4975]
- 7 Sugihara K, Kobayashi H, Kato T, Mori T, Mochizuki H, Kameoka S, Shirouzu K, Muto T. Indication and benefit of pelvic sidewall dissection for rectal cancer. *Dis Colon Rectum* 2006; **49**: 1663-1672 [PMID: 17041749 DOI: 10.1007/s10350-006-0714-z]
 - 8 Kobayashi H, Mochizuki H, Kato T, Mori T, Kameoka S, Shirouzu K, Sugihara K. Outcomes of surgery alone for lower rectal cancer with and without pelvic sidewall dissection. *Dis Colon Rectum* 2009; **52**: 567-576 [PMID: 19404054 DOI: 10.1007/DCR.0b013e3181a1d994]
 - 9 Fujita S, Yamamoto S, Akasu T, Moriya Y. Risk factors of lateral pelvic lymph node metastasis in advanced rectal cancer. *Int J Colorectal Dis* 2009; **24**: 1085-1090 [PMID: 19387660 DOI: 10.1007/s00384-009-0704-4]
 - 10 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]
 - 11 Ueno H, Mochizuki H, Hashiguchi Y, Ishiguro M, Miyoshi M, Kajiwara Y, Sato T, Shimazaki H, Hase K. Potential prognostic benefit of lateral pelvic node dissection for rectal cancer located below the peritoneal reflection. *Ann Surg* 2007; **245**: 80-87 [PMID: 17197969 DOI: 10.1097/01.sla.0000225359.72553.8c]
 - 12 Yano H, Moran BJ. The incidence of lateral pelvic side-wall nodal involvement in low rectal cancer may be similar in Japan and the West. *Br J Surg* 2008; **95**: 33-49 [PMID: 18165939 DOI: 10.1002/bjs.6061]
 - 13 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]
 - 14 Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986; **1**: 1479-1482 [PMID: 2425199 DOI: 10.1016/s0140-6736(86)91510-2]
 - 15 Platell CF. Changing patterns of recurrence after treatment for colorectal cancer. *Int J Colorectal Dis* 2007; **22**: 1223-1231 [PMID: 17393173 DOI: 10.1007/s00384-007-0306-y]
 - 16 Harris CA, Solomon MJ, Heriot AG, Sagar PM, Tekkis PP, Dixon L, Pascoe R, Dobbs BR, Frampton CM, Harji DP, Kontovounisios C, Austin KK, Koh CE, Lee PJ, Lynch AC, Warrier SK, Frizelle FA. The Outcomes and Patterns of Treatment Failure After Surgery for Locally Recurrent Rectal Cancer. *Ann Surg* 2016; **264**: 323-329 [PMID: 26692078 DOI: 10.1097/SLA.0000000000001524]
 - 17 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]
 - 18 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* 2018; **29**: iv263 [PMID: 29741565 DOI: 10.1093/annonc/mdy161]
 - 19 Torkzad MR, Pahlman L, Glimelius B. Magnetic resonance imaging (MRI) in rectal cancer: a comprehensive review. *Insights Imaging* 2010; **1**: 245-267 [PMID: 22347920 DOI: 10.1007/s13244-010-0037-4]
 - 20 Klessen C, Rogalla P, Taupitz M. Local staging of rectal cancer: the current role of MRI. *Eur Radiol* 2007; **17**: 379-389 [PMID: 17008990 DOI: 10.1007/s00330-006-0388-x]
 - 21 Al-Sukhni E, Milot L, Fruitman M, Beyene J, Victor JC, Schmock S, Brown G, McLeod R, Kennedy E. 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; **19**: 2212-2223 [PMID: 22271205 DOI: 10.1245/s10434-011-2210-5]
 - 22 Kim NK, Kim MJ, Yun SH, Sohn SK, Min JS. Comparative study of transrectal ultrasonography, pelvic computerized tomography, and magnetic resonance imaging in preoperative staging of rectal cancer. *Dis Colon Rectum* 1999; **42**: 770-775 [PMID: 10378601 DOI: 10.1007/BF02236933]
 - 23 Kim NK, Kim MJ, Park JK, Park SI, Min JS. Preoperative staging of rectal cancer with MRI: accuracy and clinical usefulness. *Ann Surg Oncol* 2000; **7**: 732-737 [PMID: 11129420 DOI: 10.1007/s10434-000-0732-3]
 - 24 Arai K, Takifuji K, Yokoyama S, Matsuda K, Higashiguchi T, Tominaga T, Oku Y, Tani M, Yamaue H. 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; **391**: 449-454 [PMID: 16847648 DOI: 10.1007/s00423-006-0066-0]
 - 25 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]
 - 26 Min BS, Kim JS, Kim NK, Lim JS, Lee KY, Cho CH, Sohn SK. Extended lymph node dissection for rectal cancer with radiologically diagnosed extramesenteric lymph node metastasis. *Ann Surg Oncol* 2009; **16**: 3271-3278 [PMID: 19763693 DOI: 10.1245/s10434-009-0692-1]
 - 27 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**: 2787-2794 [PMID: [19618244](#) DOI: [10.1245/s10434-009-0613-3](#)]
- 28 **Lim SB**, Yu CS, Kim CW, Yoon YS, Park SH, Kim TW, Kim JH, Kim JC. Clinical implication of additional selective lateral lymph node excision in patients with locally advanced rectal cancer who underwent preoperative chemoradiotherapy. *Int J Colorectal Dis* 2013; **28**: 1667-1674 [PMID: [23943283](#) DOI: [10.1007/s00384-013-1761-2](#)]
 - 29 **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](#)]
 - 30 **Ishibe A**, Ota M, Watanabe J, Suwa Y, Suzuki S, Kanazawa A, Watanabe K, Ichikawa Y, Kunisaki C, Endo I. Prediction of Lateral Pelvic Lymph-Node Metastasis in Low Rectal Cancer by Magnetic Resonance Imaging. *World J Surg* 2016; **40**: 995-1001 [PMID: [26541864](#) DOI: [10.1007/s00268-015-3299-7](#)]
 - 31 **Yamaoka Y**, Kinugasa Y, Shiomi A, Yamaguchi T, Kagawa H, Yamakawa Y, Numata M, Furutani A. Preoperative chemoradiotherapy changes the size criterion for predicting lateral lymph node metastasis in lower rectal cancer. *Int J Colorectal Dis* 2017; **32**: 1631-1637 [PMID: [28762190](#) DOI: [10.1007/s00384-017-2873-x](#)]
 - 32 **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](#)]
 - 33 **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/anticancer.13204](#)]
 - 34 **Kawai K**, Shiratori H, Hata K, Nozawa H, Tanaka T, Nishikawa T, Muro K, Ishihara S. Optimal Size Criteria for Lateral Lymph Node Dissection After Neoadjuvant Chemoradiotherapy for Rectal Cancer. *Dis Colon Rectum* 2021; **64**: 274-283 [PMID: [33395141](#) DOI: [10.1097/DCR.0000000000001866](#)]
 - 35 **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](#)]
 - 36 **Brown G**, Richards CJ, Bourne MW, Newcombe RG, Radcliffe AG, Dallimore NS, Williams GT. Morphologic predictors of lymph node status in rectal cancer with use of high-spatial-resolution MR imaging with histopathologic comparison. *Radiology* 2003; **227**: 371-377 [PMID: [12732695](#) DOI: [10.1148/radiol.2272011747](#)]
 - 37 **Tan KY**, Yamamoto S, Fujita S, Akasu T, Moriya Y. Improving prediction of lateral node spread in low rectal cancers--multivariate analysis of clinicopathological factors in 1,046 cases. *Langenbecks Arch Surg* 2010; **395**: 545-549 [PMID: [20361335](#) DOI: [10.1007/s00423-010-0642-1](#)]
 - 38 **Kinugasa T**, Akagi Y, Ochi T, Ishibashi Y, Tanaka N, Oka Y, Mizobe T, Yuge K, Fujino S, Kibe S, Shirouzu K. Lateral lymph-node dissection for rectal cancer: meta-analysis of all 944 cases undergoing surgery during 1975-2004. *Anticancer Res* 2013; **33**: 2921-2927 [PMID: [23780981](#)]
 - 39 **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](#)]
 - 40 **Ogawa S**, Hida J, Ike H, Kinugasa T, Ota M, Shinto E, Itabashi M, Okamoto T, Sugihara K. The important risk factor for lateral pelvic lymph node metastasis of lower rectal cancer is node-positive status on magnetic resonance imaging: study of the Lymph Node Committee of Japanese Society for Cancer of the Colon and Rectum. *Int J Colorectal Dis* 2016; **31**: 1719-1728 [PMID: [27576475](#) DOI: [10.1007/s00384-016-2641-3](#)]
 - 41 **Hoshino N**, Murakami K, Hida K, Sakamoto T, Sakai Y. Diagnostic accuracy of magnetic resonance imaging and computed tomography for lateral lymph node metastasis in rectal cancer: a systematic review and meta-analysis. *Int J Clin Oncol* 2019; **24**: 46-52 [PMID: [30259217](#) DOI: [10.1007/s10147-018-1349-5](#)]
 - 42 **Lambregts DM**, Beets GL, Maas M, Kessels AG, Bakers FC, Cappendijk VC, Engelen SM, Lahaye MJ, de Bruijne AP, Lammering G, Leiner T, Verwoerd JL, Wildberger JE, Beets-Tan RG. Accuracy of gadofosveset-enhanced MRI for nodal staging and restaging in rectal cancer. *Ann Surg* 2011; **253**: 539-545 [PMID: [21239980](#) DOI: [10.1097/SLA.0b013e31820b01f1](#)]
 - 43 **Koh DM**, George C, Temple L, Collins DJ, Toomey P, Raja A, Bett N, Farhat S, Husband JE, Brown G. Diagnostic accuracy of nodal enhancement pattern of rectal cancer at MRI enhanced with ultrasmall superparamagnetic iron oxide: findings in pathologically matched mesorectal lymph nodes. *AJR Am J Roentgenol* 2010; **194**: W505-W513 [PMID: [20489069](#) DOI: [10.2214/AJR.08.1819](#)]
 - 44 **Koh DM**, Brown G, Temple L, Raja A, Toomey P, Bett N, Norman AR, Husband JE. Rectal cancer:

- mesorectal lymph nodes at MR imaging with USPIO vs histopathologic findings--initial observations. *Radiology* 2004; **231**: 91-99 [PMID: [14976266](#) DOI: [10.1148/radiol.2311030142](#)]
- 45 **Lahaye MJ**, Engelen SM, Kessels AG, de Bruijne AP, von Meyenfeldt MF, van Engelshoven JM, van de Velde CJ, Beets GL, Beets-Tan RG. USPIO-enhanced MR imaging for nodal staging in patients with primary rectal cancer: predictive criteria. *Radiology* 2008; **246**: 804-811 [PMID: [18195379](#) DOI: [10.1148/radiol.2463070221](#)]
 - 46 **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](#)]
 - 47 **Catalano OA**, Lee SI, Parente C, Cauley C, Furtado FS, Striar R, Soricelli A, Salvatore M, Li Y, Umutlu L, Cañamaque LG, Groshar D, Mahmood U, Blaszkowsky LS, Ryan DP, Clark JW, Wo J, Hong TS, Kunitake H, Bordeianou L, Berger D, Ricciardi R, Rosen B. Improving staging of rectal cancer in the pelvis: the role of PET/MRI. *Eur J Nucl Med Mol Imaging* 2021; **48**: 1235-1245 [PMID: [33034673](#) DOI: [10.1007/s00259-020-05036-x](#)]
 - 48 **Suarez-Weiss KE**, Herold A, Gervais D, Palmer E, Amorim B, King JD, Weier L, Shahein T, Bernstine H, Domachevsk L, Cañamaque LG, Herrmann K, Umutlu L, Groshar D, Catalano OA. Hybrid imaging of the abdomen and pelvis. *Radiologe* 2020; **60**: 80-89 [PMID: [32424463](#) DOI: [10.1007/s00117-020-00661-x](#)]
 - 49 **Hojo K**, Sawada T, Moriya Y. An analysis of survival and voiding, sexual function after wide iliopelvic lymphadenectomy in patients with carcinoma of the rectum, compared with conventional lymphadenectomy. *Dis Colon Rectum* 1989; **32**: 128-133 [PMID: [2914526](#) DOI: [10.1007/BF02553825](#)]
 - 50 **Moriya Y**, Sugihara K, Akasu T, Fujita S. Importance of extended lymphadenectomy with lateral node dissection for advanced lower rectal cancer. *World J Surg* 1997; **21**: 728-732 [PMID: [9276704](#) DOI: [10.1007/s002689900298](#)]
 - 51 **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](#)]
 - 52 **Georgiou P**, Tan E, Gouvas N, Antoniou A, Brown G, Nicholls RJ, Tekkis P. Extended lymphadenectomy vs conventional surgery for rectal cancer: a meta-analysis. *Lancet Oncol* 2009; **10**: 1053-1062 [PMID: [19767239](#) DOI: [10.1016/S1470-2045\(09\)70224-4](#)]
 - 53 **Wang Z**, Loh KY, Tan KY, Woo EC. The role of lateral lymph node dissection in the management of lower rectal cancer. *Langenbecks Arch Surg* 2012; **397**: 353-361 [PMID: [22105772](#) DOI: [10.1007/s00423-011-0864-x](#)]
 - 54 **Amin MB**, Edge S, Greene F. AJCC cancer staging manual. 8th ed. New York, Springer; 2017
 - 55 **Sauer R**, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, Martus P, Tschmelitsch J, Hager E, Hess CF, Karstens JH, Liersch T, Schmidberger H, Raab R; German Rectal Cancer Study Group. Preoperative vs postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 2004; **351**: 1731-1740 [PMID: [15496622](#) DOI: [10.1056/NEJMoa040694](#)]
 - 56 **National Comprehensive Cancer Network**. Colon Cancer (Version 1.2021). [cited 1 February 2021] Available from: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf
 - 57 **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](#)]
 - 58 **Ozawa H**, Kotake K, Hosaka M, Hirata A, Sugihara K. Impact of Lateral Pelvic Lymph Node Dissection on the Survival of Patients with T3 and T4 Low Rectal Cancer. *World J Surg* 2016; **40**: 1492-1499 [PMID: [26908236](#) DOI: [10.1007/s00268-016-3444-y](#)]
 - 59 **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](#)]
 - 60 **Nagawa H**, Muto T, Sunouchi K, Higuchi Y, Tsurita G, Watanabe T, Sawada T. Randomized, controlled trial of lateral node dissection vs. nerve-preserving resection in patients with rectal cancer after preoperative radiotherapy. *Dis Colon Rectum* 2001; **44**: 1274-1280 [PMID: [11584199](#) DOI: [10.1007/BF02234784](#)]
 - 61 **Watanabe T**, Tsurita G, Muto T, Sawada T, Sunouchi K, Higuchi Y, Komuro Y, Kanazawa T, Iijima T, Miyaki M, Nagawa H. Extended lymphadenectomy and preoperative radiotherapy for lower rectal cancers. *Surgery* 2002; **132**: 27-33 [PMID: [12110792](#) DOI: [10.1067/msy.2002.125357](#)]
 - 62 **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](#)]
- 63 **Gao X**, Wang C, Yu Y, Singh D, Yang L, Zhou Z. Lateral lymph node dissection reduces local recurrence of locally advanced lower rectal cancer in the absence of preoperative neoadjuvant chemoradiotherapy: a systematic review and meta-analysis. *World J Surg Oncol* 2020; **18**: 304 [PMID: [33228677](#) DOI: [10.1186/s12957-020-02078-1](#)]
- 64 **Wang X**, Qiu A, Liu X, Shi Y. Total mesorectal excision plus lateral lymph node dissection vs TME on rectal cancer patients: a meta-analysis. *Int J Colorectal Dis* 2020; **35**: 997-1006 [PMID: [32356120](#) DOI: [10.1007/s00384-020-03610-1](#)]
- 65 **Ma P**, Yuan Y, Yan P, Chen G, Ma S, Niu X, Xu M, Yang K, Cai H. The efficacy and safety of lateral lymph node dissection for patients with rectal cancer: A systematic review and meta-analysis. *Asian J Surg* 2020; **43**: 891-901 [PMID: [31926817](#) DOI: [10.1016/j.asjsur.2019.11.006](#)]
- 66 **Emile SH**, Elfeki H, Shalaby M, Sakr A, Kim NK. Outcome of lateral pelvic lymph node dissection with total mesorectal excision in treatment of rectal cancer: A systematic review and meta-analysis. *Surgery* 2021; **169**: 1005-1015 [PMID: [33317903](#) DOI: [10.1016/j.surg.2020.11.010](#)]
- 67 **Hajibandeh S**, Hajibandeh S, Matthews J, Palmer L, Maw A. Meta-analysis of survival and functional outcomes after total mesorectal excision with or without lateral pelvic lymph node dissection in rectal cancer surgery. *Surgery* 2020; **168**: 486-496 [PMID: [32620303](#) DOI: [10.1016/j.surg.2020.04.063](#)]
- 68 **Law BZY**, Yusuf Z, Ng YE, Aly EH. Does adding lateral pelvic lymph node dissection to neoadjuvant chemotherapy improve outcomes in low rectal cancer? *Int J Colorectal Dis* 2020; **35**: 1387-1395 [PMID: [32504333](#) DOI: [10.1007/s00384-020-03656-1](#)]
- 69 **Yang X**, Yang S, Hu T, Gu C, Wei M, Deng X, Wang Z, Zhou Z. What is the role of lateral lymph node dissection in rectal cancer patients with clinically suspected lateral lymph node metastasis after preoperative chemoradiotherapy? *Cancer Med* 2020; **9**: 4477-4489 [PMID: [32352659](#) DOI: [10.1002/cam4.2643](#)]
- 70 **Peeters KC**, van de Velde CJ, Leer JW, Martijn H, Junggeburst JM, Kranenbarg EK, Steup WH, Wiggers T, Rutten HJ, Marijnen CA. Late side effects of short-course preoperative radiotherapy combined with total mesorectal excision for rectal cancer: increased bowel dysfunction in irradiated patients--a Dutch colorectal cancer group study. *J Clin Oncol* 2005; **23**: 6199-6206 [PMID: [16135487](#) DOI: [10.1200/JCO.2005.14.779](#)]
- 71 **Birgisson H**, Páhlman L, Gunnarsson U, Glimelius B. Occurrence of second cancers in patients treated with radiotherapy for rectal cancer. *J Clin Oncol* 2005; **23**: 6126-6131 [PMID: [16135478](#) DOI: [10.1200/JCO.2005.02.543](#)]
- 72 **Marijnen CA**, Kapiteijn E, van de Velde CJ, Martijn H, Steup WH, Wiggers T, Kranenbarg EK, Leer JW; Cooperative Investigators of the Dutch Colorectal Cancer Group. Acute side effects and complications after short-term preoperative radiotherapy combined with total mesorectal excision in primary rectal cancer: report of a multicenter randomized trial. *J Clin Oncol* 2002; **20**: 817-825 [PMID: [11821466](#) DOI: [10.1200/JCO.2002.20.3.817](#)]
- 73 **Oh HK**, Kang SB, Lee SM, Lee SY, Ihn MH, Kim DW, Park JH, Kim YH, Lee KH, Kim JS, Kim JW, Kim JH, Chang TY, Park SC, Sohn DK, Oh JH, Park JW, Ryoo SB, Jeong SY, Park KJ. Neoadjuvant chemoradiotherapy affects the indications for lateral pelvic node dissection in mid/Low rectal cancer with clinically suspected lateral node involvement: a multicenter retrospective cohort study. *Ann Surg Oncol* 2014; **21**: 2280-2287 [PMID: [24604580](#) DOI: [10.1245/s10434-014-3559-z](#)]
- 74 **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](#)]
- 75 **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? *Dis Colon Rectum* 2017; **60**: 577-585 [PMID: [28481851](#) DOI: [10.1097/DCR.0000000000000834](#)]
- 76 **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](#)]
- 77 **Akiyoshi T**, Toda S, Tominaga T, Oba K, Tomizawa K, Hanaoka Y, Nagasaki T, Konishi T, Matoba S, Fukunaga Y, Ueno M, Kuroyanagi H. Prognostic impact of residual lateral lymph node metastasis after neoadjuvant (chemo)radiotherapy in patients with advanced low rectal cancer. *BJS Open* 2019; **3**: 822-829 [PMID: [31832589](#) DOI: [10.1002/bjs5.50194](#)]
- 78 **Ogura A**, Akiyoshi T, Nagasaki T, Konishi T, Fujimoto Y, Nagayama S, Fukunaga Y, Ueno M, Kuroyanagi H. Feasibility of Laparoscopic Total Mesorectal Excision with Extended Lateral Pelvic Lymph Node Dissection for Advanced Lower Rectal Cancer after Preoperative Chemoradiotherapy. *World J Surg* 2017; **41**: 868-875 [PMID: [27730352](#) DOI: [10.1007/s00268-016-3762-0](#)]
- 79 **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](#)]
- 80 **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](#)]
 - 81 **Patel UB**, Taylor F, Blomqvist L, George C, Evans H, Tekkis P, Quirke P, Sebag-Montefiore D, Moran B, Heald R, Guthrie A, Bees N, Swift I, Pennert K, Brown G. Magnetic resonance imaging-detected tumor response for locally advanced rectal cancer predicts survival outcomes: MERCURY experience. *J Clin Oncol* 2011; **29**: 3753-3760 [PMID: [21876084](#) DOI: [10.1200/JCO.2011.34.9068](#)]
 - 82 **Birbeck KF**, Macklin CP, Tiffin NJ, Parsons W, Dixon MF, Mapstone NP, Abbott CR, Scott N, Finan PJ, Johnston D, Quirke P. Rates of circumferential resection margin involvement vary between surgeons and predict outcomes in rectal cancer surgery. *Ann Surg* 2002; **235**: 449-457 [PMID: [11923599](#) DOI: [10.1097/0000658-200204000-00001](#)]
 - 83 **São Julião GP**, Habr-Gama A, Vailati BB, Perez RO. The good, the bad and the ugly: rectal cancers in the twenty-first century. *Tech Coloproctol* 2017; **21**: 573-575 [PMID: [28631136](#) DOI: [10.1007/s10151-017-1651-7](#)]
 - 84 **Haanappel A**, Kroon HM, Schaap DP, Bedrikovetski S, Dudi-Venkata NN, Lee HX, Thomas ML, Liu J, van der Valk MJM, Rutten HJT, Beets GL, Kusters M, Samsour T. Lateral Lymph Node Metastases in Locally Advanced Low Rectal Cancers May Not Be Treated Effectively With Neoadjuvant (Chemo)Radiotherapy Only. *Front Oncol* 2019; **9**: 1355 [PMID: [31850231](#) DOI: [10.3389/fonc.2019.01355](#)]
 - 85 **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](#)]
 - 86 **Wang P**, Zhou S, Zhou H, Liang J, Zhou Z. Evaluating predictive factors for determining the presence of lateral pelvic node metastasis in rectal cancer patients following neoadjuvant chemoradiotherapy. *Colorectal Dis* 2019; **21**: 791-796 [PMID: [30801862](#) DOI: [10.1111/codi.14595](#)]
 - 87 **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](#)]
 - 88 **Matsuda T**, Sumi Y, Yamashita K, Hasegawa H, Yamamoto M, Matsuda Y, Kanaji S, Oshikiri T, Nakamura T, Suzuki S, Kakeji Y. Outcomes and prognostic factors of selective lateral pelvic lymph node dissection with preoperative chemoradiotherapy for locally advanced rectal cancer. *Int J Colorectal Dis* 2018; **33**: 367-374 [PMID: [29442155](#) DOI: [10.1007/s00384-018-2974-1](#)]
 - 89 **Nagasaki T**, Akiyoshi T, Fujimoto Y, Konishi T, Nagayama S, Fukunaga Y, Ueno M. Preoperative Chemoradiotherapy Might Improve the Prognosis of Patients with Locally Advanced Low Rectal Cancer and Lateral Pelvic Lymph Node Metastases. *World J Surg* 2017; **41**: 876-883 [PMID: [27730348](#) DOI: [10.1007/s00268-016-3748-y](#)]
 - 90 **Kim HJ**, Choi GS, Park JS, Park SY, Cho SH, Lee SJ, Kang BW, Kim JG. Optimal treatment strategies for clinically suspicious lateral pelvic lymph node metastasis in rectal cancer. *Oncotarget* 2017; **8**: 100724-100733 [PMID: [29246016](#) DOI: [10.18632/oncotarget.20121](#)]
 - 91 **Chen JN**, Liu Z, Wang ZJ, Mei SW, Shen HY, Li J, Pei W, Wang Z, Wang XS, Yu J, Liu Q. Selective lateral lymph node dissection after neoadjuvant chemoradiotherapy in rectal cancer. *World J Gastroenterol* 2020; **26**: 2877-2888 [PMID: [32550762](#) DOI: [10.3748/wjg.v26.i21.2877](#)]
 - 92 **Yahya JB**, Herzig DO, Farrell MJ, Degnin CR, Chen Y, Holland J, Brown S, Jaboin J, Tsikitis VL, Lu K, Thomas CR Jr, Mitin T. Does a fine line exist between regional and metastatic pelvic lymph nodes in rectal cancer-striking discordance between national guidelines and treatment recommendations by US radiation oncologists. *J Gastrointest Oncol* 2018; **9**: 441-447 [PMID: [29998009](#) DOI: [10.21037/jgo.2018.02.05](#)]
 - 93 **Malakorn S**, Chang GJ. Treatment of rectal cancer in the East and West: Should it be different? *Surgery* 2017; **162**: 315-316 [PMID: [28619666](#) DOI: [10.1016/j.surg.2017.04.002](#)]
 - 94 **Samsour T**, Chang GJ. Lateral Node Dissection in Low Rectal Cancer: Time for a Global Approach? *Ann Surg* 2017; **266**: 208-209 [PMID: [28437315](#) DOI: [10.1097/SLA.0000000000002273](#)]
 - 95 **Samsour T**, Chang GJ. Lateral pelvic lymph node dissection and radiation treatment for rectal cancer: Mutually exclusive or mutually beneficial? *Ann Gastroenterol Surg* 2018; **2**: 348-350 [PMID: [30238075](#) DOI: [10.1002/ags3.12197](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

