



Lateral lymph node dissection and urogenital function with and without neoadjuvant treatment

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Comment on: Jiang Y, Zhou S, Pei W, *et al.* Does neoadjuvant chemoradiotherapy increase the effect of lateral lymph node dissection on urogenital function? *Transl Cancer Res* 2022. doi: 10.21037/tcr-22-87

Submitted Apr 12, 2022. Accepted for publication Apr 18, 2022.

doi: 10.21037/tcr-22-1023

View this article at: <https://dx.doi.org/10.21037/tcr-22-1023>

Lateral lymph node metastasis (LLNM) is present in patients with 10% to 25% in patients with locally advanced rectal cancer (LARC) (1). This lateral compartment can be found on the obturator artery, internal iliac, and medial aspect of the external iliac artery. Patients with LLNM present higher rates of recurrence and worse overall survival. For decades, lateral pelvic nodes (LPN) have been considered and treated as metastatic diseases, rather than local in nearly all Western countries. In addition, it has been suggested that neoadjuvant chemoradiation and total mesorectal excision (TME) alone may be insufficient treatment for patients with clinically positive nodes (2).

Lateral pelvic lymph node dissection (LPLD) in appropriate patients has important benefits prognosis and decreasing lateral local recurrence (3). The anatomical considerations of this area are critical to understand in treating patients with extramesorectal extension and by the salvage of patients with lateral recurrence. LPLD in addition to TME has shown survival rates more consistent with N2a/N2b mesorectal node involvement and better than that of stage IV cancers. As such, a greatly renewed interest in surgical lymphadenectomy of the lateral compartment in conjunction with TME has swept through Europe and trickled into the Americas over the last 5 years. However, the optimal approach for the treatment of LPN remains a topic of great interest and debate.

The management of rectal cancer has continued to rapidly evolve utilizing systemic chemotherapy, combined chemoradiotherapy, and increasing by refined surgery to maximize cure and survival, while minimizing morbidity, and local recurrence. Although disease free survival and avoidance of permanent stoma are objective outcomes and readily tracked, the incidence of bowel, urologic, and sexual function and other patient reported outcomes have been generally under evaluated (4).

However, the following thoughts seem non-equivocal and intuitive. Every tumor directed therapy for rectal cancer, while potentially aiding in survival, also carries some functional consequences. Pelvic radiation therapy comprises a vital component in the management of rectal cancer delivering high doses of radiation to the tumor and local regional lymph nodes while attempting to minimize collateral damage to surrounding tissues and organs. Advances in the delivery of radiation such as intensity modulated radiation therapy (IMRT) have reduced toxicity, yet nonetheless toxicity side effects remain real. Precise TME, while excellent at tumor control, has significant effects on gastrointestinal function and less so on sexual and urologic function. One must even consider the effect of chemotherapy on the peripheral nervous system and continence, given the increased use of system NAT which are often limited by neuropathy (5). The addition of LPLD,

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nearby the autonomic pelvic plexus, seems like an obvious independent risk for genitourinary dysfunction (4).

Secondly, the effects of each of these interventions are cumulative and commonly irreversible while local excision nearly preserves pelvic function this is perhaps at the cost increased risk of local recurrence. Patients determined to have a complete clinical response and organ preservation still have a relatively high incidence of bowel dysfunction as well as genitourinary symptoms (6). However, this is dramatically improved compared to those patients which undergo chemoradiation and surgery. Similarly, those who undergo upfront surgery omitting chemoradiotherapy are better off functionally than patients undergoing all treatment modalities.

Clinical studies in rectal cancer have similarly evolved with the intent to avoid overtreatment while maximizing response. The OPRA trial (7) sought to maximize total neoadjuvant treatment (NAT) to avoid rectal resection, while the United States based PROSPECT study (8) sought to determine if survival was equivalent in those patients undergoing initial induction chemotherapy, downstaging, and avoidance of radiotherapy.

LPLD is associated with a longer operation time, greater blood loss and may severely impair both urinary and sexual function, compromising patient quality of life. However, minimally invasive techniques for LPLD have potentially effectively reduced operating time, with a drastic reduction in blood loss and excellent preservation of urinary function. One would also expect improvement in functional outcomes related to surgeon experience, volume, and expertise in LPLD. Over the 40 years Japan has been at the forefront of this technique recommending routine bilateral LPND in all cT3 and cT4 tumors initially, while now evolving to a more selective approach (9). Several recent retrospective studies including the work done by the International Consortium on Pelvic Lymphadenectomy have determined the optimal preoperative short axis diameter for indication for LPND as 37 mm. Utilizing this size cutoff criteria, more than 60% of patients were spared the morbidity of lymphadenectomy, while decreasing lateral recurrence rates from 19.5% to 5.7% (10).

Clearly, a selective approach to LPLD provides a more optimal strategy in balancing the benefits of LPLD against potential morbidity and functional deficits. Advancements and standardization of the radiologic determination of pathologic lateral nodes are critical to further defining and standardizing indications and patient selection. Improving

surgical outcomes through adequate training, mentoring, and proctoring by qualified surgeons will likely further minimize disparity in outcomes and once again highlights the challenges in the training schema of new surgical techniques.

The result of another study shows significant differences in urinary and sexual function between patients who underwent LPLD and those who underwent only TME resection (11). These results are not surprising, as the autonomic nerves are more vulnerable to injury during LPLD. However, previous studies have shown no difference in the incidence of urinary incontinence between TME plus additional LPLD.

Despite the challenges and limitations of scientific studies we should continue to evaluate the optimal strategy for the treatment of the lateral pelvic lymph nodes keeping in mind the functional outcomes for our patients.

Jiang *et al.* carried out a remarkably interesting retrospective study with a total of 145 patients that were enrolled, of these 39 were excluded due to preoperative urogenital dysfunction or lack of follow-up (12). A total of 106 patients who underwent TME+LPLD surgery for mid-low rectal cancer were separated into two groups based on whether they had received neoadjuvant chemoradiotherapy (n=51) or not (n=55).

One detail with this study is the insufficient explanation for the indication of NAT. If all the patients had mid and low rectal cancer with LLNM, it is difficult to understand how the treatment was made for each patient.

Another crucial point is the relatively small group of patients, it is unlikely to detect outcome differences in this group. On the other hand, it is exceedingly difficult to reach this number of specific patients (LLNM and LPLD with or without NAT) to perform a single center study.

Obviously, a well conducted large-scale multi-center prospective study will be required to back up these findings.

Another important characteristic with this study is the fact that does not analyzed the sexual dysfunction on the female group, the authors affirm that's because women are less likely than men to give information to their physician about difficulties relating to their sexuality. Especially in some cultures women are too hesitant to comply well with questions about sexual dysfunction during follow-up due to cultural pressures.

Many studies, as this one, are retrospective in nature with the normal occurring limitations and bias as well as cultural limitations and discomfort with patient reporting

despite valiant attempts at validated patient questionnaires and minimizing confounding factors.

In the conclusion of the study, NAT was not related to a significantly higher rate of urogenital dysfunction. In addition, the distance between the tumor and the anal margin was associated to the occurrence of urine failure, and age was an independent predictor of male sexual dysfunction.

Finally, this topic brings the discussion about the appropriate LPN size cutoff to treat these patients with or without NAT, and the rate of compromised LLNM after resection that really developed lateral compartment or systemic recurrence.

This is one of the most important and actual topics of discussion in rectal cancer, it is our duty to perform more and better research about LPLD, and the different variables that this remarkably interesting and controversial subject brings to the recurrence and survival of our patients and how we can improve the oncological outcomes.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-1023/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Weiser MR. AJCC 8th Edition: Colorectal Cancer. *Ann Surg Oncol* 2018;25:1454-5.
2. Kim MJ, Hur BY, Lee ES, et al. 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.
3. Longchamp G, Meyer J, Christou N, et al. Total mesorectal excision with and without lateral lymph node dissection: a systematic review of the literature. *Int J Colorectal Dis* 2020;35:1183-92.
4. Yang B, Huang J, Zhou S, et al. Laparoscopic versus open selective lateral pelvic lymph node dissection following total mesorectal excision for locally advanced low rectal cancer. *Int J Colorectal Dis* 2020;35:1301-9.
5. Cercek A, Goodman KA, Hajj C, et al. Neoadjuvant chemotherapy first, followed by chemoradiation and then surgery, in the management of locally advanced rectal cancer. *J Natl Compr Canc Netw* 2014;12:513-9.
6. Jorge JMN, Habr-Gama A, Bustamante-Lopez LA. Effects of radiation therapy for rectal cancer on anorectal function. Available online: https://www.researchgate.net/publication/283818721_Effects_of_Radiation_Therapy_for_Rectal_Cancer_on_Anorectal_Function
7. Garcia-Aguilar J, Patil S, Kim JK, et al. Preliminary results of the organ preservation of rectal adenocarcinoma (OPRA) trial. *J Clin Oncol* 2020;38:4008.
8. Bossé D, Mercer J, Raissouni S, et al. PROSPECT Eligibility and Clinical Outcomes: Results From the Pan-Canadian Rectal Cancer Consortium. *Clin Colorectal Cancer* 2016;15:243-9.
9. Tsukamoto S, Fujita S, Ota M, et al. 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;107:586-94.
10. Yamaoka Y, Kinugasa Y, Shiomi A, et al. Preoperative chemoradiotherapy changes the size criterion for predicting lateral lymph node metastasis in lower rectal cancer. *Int J Colorectal Dis* 2017;32:1631-7.
11. Fujita S, Mizusawa J, Kanemitsu Y, et al. Mesorectal Excision With or Without Lateral Lymph Node Dissection for Clinical Stage II/III Lower Rectal Cancer (JCOG0212): A Multicenter, Randomized

- Controlled, Noninferiority Trial. *Ann Surg* 2017;266:201-7.
12. Jiang Y, Zhou S, Pei W, et al. Does neoadjuvant

chemoradiotherapy increase the effect of lateral lymph node dissection on urogenital function? *Transl Cancer Res* 2022. doi: 10.21037/tcr-22-87

Cite this article as: Bustamante-Lopez LA, Albert M, Monson JRT. Lateral lymph node dissection and urogenital function with and without neoadjuvant treatment. *Transl Cancer Res* 2022;11(4):599-602. doi: 10.21037/tcr-22-1023