



Evaluation of National Surgical Practice for Lateral Lymph Nodes in Rectal Cancer in an Untrained Setting: Time to Collaborate for Universal Consensus and Training Programs

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Modern surgical care of rectal cancer with neoadjuvant chemoradiotherapy and total mesorectal excision (TME) improved tumor eradication in the central pelvis, and a major cause of local recurrence is now shifting to lateral lymph node metastasis, particularly when the patients have enlarged lateral lymph nodes.¹ However, lateral lymph node dissection has not been widely performed as a common practice for rectal cancer outside of Japan and Korea, and its benefits have been a topic of controversies between the West and East. Challenges against this procedure include technical difficulty with a high risk of bleeding and postoperative complications with increased urinary and sexual dysfunction. From an oncologic standpoint, surgeons often assume that lateral lymph node metastasis is not regional but highly associated with distant metastasis, hence surgical intervention adds little, given chemoradiotherapy controls majority of lateral nodal recurrence. Contrary to such common assumptions, a recent international multicenter observational study by the Lateral Node Consortium suggested oncologic benefits of adding lateral lymph node dissection to TME after chemoradiotherapy.² The study reported a high lateral local recurrence rate of 19.5 % in patients with enlarged (≥ 7 mm) lateral lymph nodes who were treated with chemoradiotherapy followed by TME alone, whereas the rate was only 5.7 % in patients receiving TME plus lateral lymph node dissection. Further, presence of enlarged lymph nodes

was not associated with distant metastasis, suggesting that lateral nodal disease is regional and not systemic.

The work by Sluckin et al. in this issue of *Annals of Surgical Oncology*³ reported outcomes of lateral lymph node dissection from a Dutch national cross-sectional cohort study on rectal cancer surgery in 2016, aiming to evaluate the application of surgical procedures for suspicious lateral lymph nodes in an untrained setting at a national level. The authors demonstrated only one-third of patients with primarily enlarged (≥ 7 mm short-axis on MRI) lateral lymph nodes underwent surgical dissection, mostly with node-picking techniques, and such a procedure in an untrained setting resulted in high lateral local recurrence rates of 14–20 %. The authors deserve praise for pursuing the first large-scale nationwide project outside of Asia that investigated outcomes of lateral lymph node dissection in a setting of modern neoadjuvant chemoradiotherapy. Notably, the study involved radiologists to re-review all the baseline and restaging MRI images using a pre-defined protocol.

What are the clinical implications of this study that showed inconsistent results from the Lateral Node Consortium study in that lateral lymph node dissection had no oncologic benefits? Obviously, this retrospective study is subject to unadjustable selection bias toward poorer biology in the cohort receiving lateral lymph node dissection given that 174 out of 3057 overall enrolled patients with rectal cancer had enlarged lateral lymph nodes, and only 64 received lateral lymph node dissection. Acknowledging such a selection bias, this study highlighted multiple important clinical issues to be addressed on this topic.

The first issue is how to establish universal technical standardization. The study elucidated challenging environments in the real-world practice to acquire experiences on lateral lymph node dissection. The majority of Dutch

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patients with primary enlarged lateral lymph nodes were not treated surgically, and surgery, if performed, mainly consisted of less than formal node picking. Only 28 of the 69 Dutch centers performed lateral lymph node dissection, with an average number of 2.29 surgeries a year per center. Another study by the authors⁴ showed less than half of the Dutch surgeons had performed lateral lymph node dissection in the past 5 years. In 2016, there were very limited sources on how to perform complete dissection of the lateral compartment. It is not surprising that incomplete dissection with node-picking techniques resulted in failure to achieve curative clearance of metastatic lymph nodes. Incomplete nodal clearance was also suggested by very low rates of pathologic positive nodes in the study. The study suggested such incomplete nodal clearance with node picking or partial regional dissection in patients with enlarged lateral lymph nodes resulted in even higher recurrence rates compared with surgery without lateral lymph node dissection. Currently, multiple video articles using a minimally invasive approach are available.⁵ Cadaver training programs and proctor systems led by an academic surgical society will be useful to safely install a new surgical procedure as it worked in transanal TME. Of note, common areas of lateral lymph node metastasis in rectal cancer are located deeper than those in gynecologic or urologic cancers, and ideally colorectal surgeons should perform this procedure in rectal cancer rather than urologists or gynecologists. The authors' group is now conducting a prospective LaNoReC study⁶ to investigate outcomes of lateral lymph node dissection in a setting of total neoadjuvant therapy, and participating Dutch surgeons undergo cadaveric trainings with periodical video reviews in collaboration with international experts.

The second issue is how to establish appropriate indication. This study appropriately included patients with mid-low rectal cancer within 8 cm from the anal verge, which corresponds to the level of peritoneal reflection. A national registry data from Japan clearly indicated that lateral lymph node metastasis occurs mostly in cT3–4 mid-low rectal cancer extending below the peritoneal reflection.⁷ Enlarged lateral lymph nodes in the settings of high rectal cancer or cT1–2 cancer are more likely benign. Another consideration is response to neoadjuvant chemoradiotherapy. Although persistently enlarged lateral lymph nodes after neoadjuvant therapy often carry residual metastasis and need surgical dissection, whether initially enlarged but responsive lymph nodes after neoadjuvant therapy need dissection has been controversial.^{8,9} Lateral nodal disease with bilateral metastasis, three or more metastases, and metastasis outside of the obturator and internal iliac areas are associated with poorer prognosis and need cautious selection. In the era of total neoadjuvant therapy with improved response rates, further international collaborative studies are warranted to identify the patients who benefit from this procedure.

Lastly, appropriate training of radiologists is crucial to precisely diagnose lateral nodal disease. It is important to establish a universal consensus on anatomical definitions that are understandable and sharable among radiologists, radiation oncologists, and surgeons. Interestingly, anatomical definition on the obturator and internal iliac areas are inconsistent among the guidelines for surgeons and radiation oncologists.¹⁰ Such inconsistencies are confusing for radiologists and potentially mislead surgical indication given a principle that lateral lymph node dissection is indicated for metastasis in the internal iliac and obturator areas.¹¹ Universal radiologic guidelines with an MRI atlas are warranted.

The study highlighted the importance of nationwide efforts that involve surgeons and other departments as one team, and the authors are acting as an excellent role model for improving surgical care of lateral nodal disease. Further international pan-departmental efforts are encouraged to create universal consensus and training programs to address these issues.

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