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Commentary: How far would you go?

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Esophagectomy with lymphadenectomy, plus or minus neoadjuvant chemoradiation, remains the standard of care for patients with localized esophageal cancer. Although current National Comprehensive Cancer Network Guidelines recommend a minimum of 15 lymph nodes (LN) be submitted for pathologic evaluation, questions regarding the location and extent of LN harvest persist.¹

In this thoughtful discussion, Altorki² proposes a new standardized nomenclature for esophageal cancer lymphadenectomy and considers the results of a randomized controlled trial by Li and colleagues³ from the Fudan University Group. That trial evaluated survival between 2- and 3-field LN dissection for cT1 through cT3/N0, N1 squamous cell carcinoma of the esophagus.³ Although results from the trial showed no difference in survival between the 2 groups, Altorki² addresses important limitations. In particular, he highlights the significance of the nomenclature for lymphadenectomy used by Li and colleagues,³ arguing that their definition of 2-field lymphadenectomy, which included dissection of LNs along both recurrent laryngeal nerves (RLN), is actually an extended 2-field lymphadenectomy, which may account for the similarity in survival.

Because the majority of squamous cell carcinoma is located in the upper two-thirds of the esophagus, cervical and RLN nodes may be considered regional instead of distant metastases. Adenocarcinoma, the most common histologic subtype in the United States, predominantly occurs in the distal third of the esophagus, making the benefit of a more extensive nodal dissection less clear. Studies

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CENTRAL MESSAGE

Although a standardized nomenclature system for esophageal cancer nodal stations is necessary, the benefit of extended lymphadenectomy for esophageal adenocarcinoma is still unknown.

performed on junctional and Siewert type I cancers have shown metastatic rates >10% to the supracarinal LNs, but only 1% to 2% in Siewert type II cancers.⁴⁻⁶

Further complicating the need for extended lymphadenectomy is the use of neoadjuvant therapy. Since the publication of the Neoadjuvant Chemoradiotherapy Plus Surgery versus Surgery Alone for Oesophageal or Junctional Cancer (CROSS) trial, the majority of patients with esophageal cancer receive neoadjuvant chemoradiation.^{7,8} The patients in the CRO CROSS trial who received neoadjuvant therapy had significantly fewer LNs resected with no influence on survival with an extended lymphadenectomy. However, for patients who underwent surgery alone, there was a significant survival benefit to an extended lymphadenectomy.⁹ This continues to be an area of debate with other studies showing a benefit to lymphadenectomy postinduction therapy, although consistently less influential than in those who undergo surgery alone.^{10,11}

In addition, implications regarding routine dissection of the RLN nodes are unknown. The Society of Thoracic Surgeons classifies RLN paresis as a major morbidity after esophagectomy.¹² All patients in the Fudan trial underwent an open approach, which may have provided the ability to safely perform a 3-field dissection with lower risk of complications.³ However, with strong evidence showing the benefits of minimally invasive surgery, more esophagectomies within the United States are now being performed by a minimally invasive approach.¹³⁻¹⁵

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Adopting an extended lymphadenectomy in the era of minimally invasive surgery and neoadjuvant therapy may be hard for many to embrace. The community of surgeons treating esophageal cancer eagerly await the results of the Distribution of Lymph Node Metastases in Esophageal Carcinoma trial to help answer many of these questions.¹⁶ Until we have comparable data regarding histology and number and location of LNs resected in patients with and without induction therapy, these questions will remain unanswered.

References

1. Ajani JA, D'Amico TA, Bentrem DJ, Chao J, Corvera C, Das P, et al. Esophageal and esophagogastric junction cancers, version 2.2019, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2019;17:855-83.
2. Altorki N. Two-field lymph node dissection or three-field lymph node dissection. What's in a name? *J Thorac Cardiovasc Surg*. 2022;163:1695-7.
3. Li B, Zhang Y, Miao L, Ma L, Luo X, Zhang Y, et al. Esophagectomy with three-field versus two-field lymphadenectomy for middle and lower thoracic esophageal cancer: long-term outcomes of a randomized clinical trial. *J Thorac Oncol*. 2021;16:310-7.
4. Leers JM, DeMeester SR, Chan N, Ayazi S, Oezcelik A, Abate E, et al. Clinical characteristics, biologic behavior, and survival after esophagectomy are similar for adenocarcinomas of the gastroesophageal junction and the distal esophagus. *J Thorac Cardiovasc Surg*. 2009;138:594-602.
5. Rüdiger Siewert J, Feith M, Werner M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. *Ann Surg*. 2000;232:353-61.
6. Parry K, Haverkamp L, Bruijnen RC, Siersema PD, Ruurda JP, van Hillegersberg R. Surgical treatment of adenocarcinomas of the gastro-esophageal junction. *Ann Surg Oncol*. 2015;22:597-603.
7. Van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366:2074-84.
8. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. *Lancet Oncol*. 2015;16:1090-8.
9. Talsma K, Wijnhoven B, van Lanschot J, van Berge Henegouwen M. Impact of neoadjuvant chemoradiation on lymph node status in esophageal cancer: post hoc analysis of a randomized controlled trial. *Ann Surg*. 2017;266:e52-3.
10. Samson P, Puri V, Broderick S, Patterson GA, Meyers B, Crabtree T. Extent of lymphadenectomy is associated with improved overall survival after esophagectomy with or without induction therapy. *Ann Thorac Surg*. 2017;103:406-15.
11. Chen D, Mao Y, Xue Y, Sang Y, Liu D, Chen Y. Does the lymph node yield affect survival in patients with esophageal cancer receiving neoadjuvant therapy plus esophagectomy? A systematic review and updated meta-analysis. *E Clin Med*. 2020;25:100431.
12. Raymond DP, Seder CW, Wright CD, Magee MJ, Kosinski AS, Cassivi SD, et al. Predictors of major morbidity or mortality after resection for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. *Ann Thorac Surg*. 2016;102:207-14.
13. Yerokun BA, Sun Z, Yang CJ, Gulack BC, Speicher PJ, Adam MA, et al. Minimally invasive versus open esophagectomy for esophageal cancer: a population-based analysis. *Ann Thorac Surg*. 2016;102:416-23.
14. Ahmadi N, Crnic A, Seely AJ, Sundaresan SR, Villeneuve PJ, Maziak DE, et al. Impact of surgical approach on perioperative and long-term outcomes following esophagectomy for esophageal cancer. *Surg Endosc*. 2018;32:1892-900.
15. Zheng R, Tham EJH, Rios-Diaz AJ, Grenda TR, Evans NR III, Rosato EL, et al. A 10-year ACS-NSQIP analysis of trends in esophagectomy practices. *J Surg Res*. 2020;256:103-11.
16. Hagens ERC, van Berge Henegouwen MI, van Sandick JW, Cuesta MA, van der Peet DL, Heisterkamp J, et al. Distribution of lymph node metastases in esophageal carcinoma [TIGER study]: study protocol of a multinational observational study. *BMC Cancer*. 2019;19:662.