More isn't always better...but sometimes it is

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Central Message

Li and colleagues describe a post hoc analysis of patients with node-positive esophageal squamous cell carcinoma, demonstrating extended lymph node dissection is associated with improved survival.

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In this issue of the *Journal*, Li and colleagues¹ present a post hoc subgroup analysis of their randomized trial, in which they compared extended radical versus standard lymphadenectomy in patients undergoing surgery for node-positive squamous cell carcinoma of the esophagus. Their analysis ultimately demonstrates that patients undergoing extended lymphadenectomy had improved 5-year overall (51% vs 31%) and disease-free (40% vs 26%) survival. Interestingly, although the cumulative rates of recurrence were similar between groups through the duration of the study (58% for extended vs 55% for standard lymphadenectomy), the patterns of recurrence were markedly different. Locoregional recurrence was twice as frequent in patients undergoing standard lymphadenectomy than in those undergoing extended resection (23% vs 11%), whereas distant or mixed recurrence occurred more often in the extended than the standard lymphadenectomy group (47% vs 32%). On the basis of these data, it would seem that extended lymphadenectomy may offer enhanced local control of disease; however, the presence or absence of distant metastases may ultimately determine long-term survival in the majority of patients.

Although the findings from this study are important and add to the existing data demonstrating that lymph node dissection plays an important role in achieving accurate staging and treatment of patients with esophageal cancer, several points should be considered when interpreting these results.²⁻⁴ Although the data in this study were derived from a randomized clinical trial, the analysis itself was performed post hoc on only a subgroup of patients with positive lymph nodes on final pathologic analysis. Therefore, the advantages of randomization are compromised to some degree, and the authors themselves highlight several ways in which the cohorts differed (American Society of Anesthesiologists score, body mass index, tumor location, etc). Similarly, as there were no statistically significant differences in survival in the overall population from the randomized trial, it remains

unclear whether more-extensive dissection would be associated with a benefit in unselected patients. Extended lymphadenectomy might therefore be used in patients with suspicious nodes on preoperative imaging or intraoperative examination. The authors suggest frozen section analysis to inform intraoperative decision-making. Although intraoperative assessment of suspicious nodes might be useful, systematic analysis of 20 or more nodes removed during the standard dissection would be tedious and burdensome.

In addition, although the analysis focuses on extended versus standard lymph node dissection, the trial is really an examination of 2 different operative techniques. The extended lymphadenectomy is an Ivor Lewis procedure including an abdominal phase (with dissection of the common hepatic and celiac lymph nodes) and a right thoracotomy. "Extended lymphadenectomy" specifically refers to systematic dissection of the upper mediastinal lymph nodes, including those along the bilateral recurrent laryngeal nerves, performed during this procedure. The standard lymphadenectomy is performed through a left thoracotomy, with mobilization of the left diaphragm to facilitate abdominal dissection. Of note, the celiac and common hepatic nodes were not routinely dissected during this procedure, and the upper mediastinal nodes were removed if accessible (but not systematically cleared). Although the rates of recurrence in the upper abdominal lymph nodes were similar between groups and margin positivity (R1/R2) was somewhat high in both groups (37.5% vs 40%), other technical differences in these approaches may affect outcomes.

Last, it is important to note that these patients were treated with primary surgery followed by adjuvant chemotherapy or radiation if indicated. It is unclear whether these data can be extrapolated to patients receiving neoadjuvant chemotherapy or chemoradiation.⁵ It is possible that the use of induction therapy may result in nodal sterilization in the mediastinum and perhaps lessen the need for extensive lymphadenectomy. It is also unclear whether this study would be applicable to patients with adenocarcinoma.

In conclusion, this study by Li and colleagues¹ is an important contribution to the literature regarding the utility of a thorough lymph node dissection in patients with esophageal cancer. Whether these benefits are conferred through more-accurate staging or the therapeutic implications of node removal remains debatable. Nonetheless, the impact on patient outcomes in this study and others provides strong evidence that a thorough lymphadenectomy benefits

patients. Li and colleagues¹ should be congratulated on their completion of a randomized study in the surgical treatment of esophageal cancer and their informative post hoc analysis presented here.

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