Proceed with caution: The importance of surveillance in patients with pathologic complete response after chemoradiation therapy plus surgery for esophageal cancer

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Central Message

Surveillance strategies for patients with clinical stage II or III esophageal cancer with pathologically complete response after trimodality therapy may need to be stratified by histologic subtype.

See Article page 1249.

Patients with a pathologic complete response (pCR) after trimodality therapy for esophageal cancer have improved disease-free and overall survivals relative to those without a pCR. Despite this improvement in survival, approximately one-quarter of patients with a pCR have a recurrence.^{1,2} Identifying these recurrences is important, because salvage therapy is associated with improved survival.³ Almost half of patients who receive salvage chemoradiation therapy for locoregional recurrence survive beyond 2 years, and even those with distant recurrence have an improvement in survival.³

Unfortunately, there are no guidelines delineating a surveillance strategy for patients with esophageal cancer that are based on high-level evidence. The National Comprehensive Cancer Network (NCCN) guidelines provide some guidance for stage-specific surveillance; these are based on available data, which are entirely retrospective, and panel member recommendations. For patients with stage II or III esophageal cancer treated with trimodality therapy, esophagogastroduodenoscopic surveillance is not recommended, because anastomotic recurrence is uncommon. The NCCN recommends chest and abdomen computed tomography with contrast every 6 months for up to 2 years, because the literature, at least as of 2014, indicated that 90% of recurrences occur within 36 months of surgery.

Interestingly, the NCCN guidelines state that recurrences in patients with a pCR are not frequent, but one-quarter of patients with pCR have a recurrence.^{1,2} Furthermore, NCCN surveillance strategies are stratified by tumor classification (T and N stage) as well as type of therapy, but not by histologic type. Moreover, the guidelines are based on literature up to and including 2014. Since then, additional retrospective studies from high-volume centers have contributed to our understanding of recurrence in the setting of pCR after trimodality therapy for esophageal cancer,^{3,4} such as the study by Barbetta and colleagues¹ in this

issue of *The Journal of Thoracic and Cardiovascular Surgery*, which focuses exclusively on recurrence in these patients. In this study, 61 of 233 patients with a pCR after trimodality therapy had a recurrence and the cumulative incidence of recurrence did not differ by histology. Those with adenocarcinoma had a higher incidence of distant recurrence, however, whereas those with squamous cell carcinoma had a higher incidence of locoregional recurrence, with mediastinal lymph nodes being the most frequent site. These findings differ from previous work demonstrating no significant difference in recurrence patterns between patients with pCR with adenocarcinoma and those with squamous cell carcinoma.^{4,5} Moreover, Barbetta and colleagues¹ report that poor tumor differentiation was an independent predictor of recurrence in all patients with a pCR and that higher clinical stage was also associated with recurrence for those with adenocarcinoma. These data suggest that surveillance guidelines should be stratified by both histologic type and whether pCR was achieved. Surveillance strategies for patients who underwent trimodality therapy for locally advanced esophageal cancer are a work in progress, and although high-quality retrospective studies have been published, perhaps these studies can be used to guide prospective work that can be used to inform surveillance

best practices. Furthermore, because poor tumor differentiation is associated with recurrence, studies focusing on predictors of recurrence beyond clinicopathologic factors—for example, tumor molecular characteristics—are needed.

References

1. Barbetta A, Sihag S, Nobel T, Hsu M, Tan KS, Bains M, et al. Patterns and risk of recurrence in esophageal cancer patients with a pathological complete response after chemotherapy followed by surgery. *J Thorac Cardiovasc Surg*. 2019;157:1249-59.
2. Luc G, Gronnier C, Lebreton G, Brigand C, Mabrut JY, Bail JP, et al. Predictive factors of recurrence in patients with pathological complete response after esophagectomy following neoadjuvant chemoradiotherapy for esophageal cancer: a multicenter study. *Ann Surg Oncol*. 2015;22(Suppl 3):S1357-64.
3. Xi M, Hallemeier CL, Merrell KW, Liao Z, Murphy MA, Ho L, et al. Recurrence risk stratification after preoperative chemoradiation of esophageal adenocarcinoma. *Ann Surg*. 2017;268:289-95.
4. Xi M, Yang Y, Zhang L, Yang H, Merrell KW, Hallemeier CL, et al. Multi-institutional analysis of recurrence and survival after neoadjuvant chemoradiotherapy of esophageal cancer: impact of histology on recurrence patterns and outcomes. *Ann Surg*. January 12, 2018 [Epub ahead of print].
5. Valböhmer D, Hölscher A, DeMeester S, DeMeester T, Salo J, Peters J, et al. A multicenter study of survival after neoadjuvant radiotherapy/chemotherapy and esophagectomy for ypT0N0M0R0 esophageal cancer. *Ann Surg*. 2010;252:744-9.