

Editorial

Esophageal cancer: Is preoperative chemoradiation the new standard?

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Most patients with esophageal cancer require multi-disciplinary management, with radiation therapy constituting a key component of therapy. In this issue, Jabbour et al. present an excellent review article on the role of radiation therapy in the postoperative management of esophageal cancer (1). The authors must be commended for this thorough, evidence-based review article. In addition to discussing postoperative radiotherapy for esophageal cancer, the authors also discuss the roles of definitive chemoradiation, preoperative chemoradiation, preoperative chemotherapy and postoperative chemotherapy.

As Jabbour et al. have discussed, multiple randomized trials have evaluated whether preoperative chemoradiation improves outcomes compared to surgery alone for esophageal cancer (1). In the Cancer and Leukemia Group B (CALGB) 9781 trial, patients with T1-T3 esophageal squamous cell carcinoma or adenocarcinoma were randomized to receive either surgery alone, or surgery with preoperative chemoradiation, with a dose of 50.4 Gy in 1.8 Gy fractions, along with concurrent cisplatin and 5-fluorouracil (2). Patients in the preoperative chemoradiation arm had a median survival of 4.5 years and a 5-year survival of 39%, while patients in the surgery alone arm had a median survival of 1.8 years and a 5-year survival of 16% ($P=0.002$). However, it should be noted that this trial had a poor accrual of only 56 patients, out of a planned accrual of 475 patients.

The case for preoperative chemoradiation has been recently

bolstered by presentation of results from the CROSS trial from the Netherlands (3). In this phase III trial, 363 patients with T2-3 N0-1 esophageal carcinoma were randomized to receive either surgery alone, or surgery with preoperative chemoradiation, with a dose of 41.4 Gy in 1.8 Gy fractions, with concurrent paclitaxel (50 mg/m²) and carboplatin (AUC 2). Of the enrolled patients, 75% had adenocarcinoma, 24% had squamous cell carcinoma, and 1% had other histologies. Overall survival was significantly improved in the preoperative chemoradiation arm ($P=0.01$). Patients in the preoperative chemoradiation arm had a median survival of 49 months and a 3-year survival of 59%, whereas patients in the surgery alone arm had a median survival of 26 months and a 3-year survival of 48%. Formal publication of this trial is being eagerly awaited. Nevertheless, this trial has the potential of being regarded as a landmark study, which will pave the way for establishing preoperative chemoradiation as a standard of care for resectable esophageal cancer.

Jabbour et al. have included a detailed discussion on the relative advantages and disadvantages of preoperative and postoperative therapy. An important advantage of preoperative chemoradiation is that smaller fields can be used in most cases. With postoperative chemoradiation, the field has to be expanded to include the anastomosis, which can potentially lead to higher rates of toxicity.

While preoperative chemoradiation is likely to play an increasingly important role in the management of resectable esophageal cancer, postoperative chemoradiation will also continue to play a role. Since clinical staging is not always accurate, some patients deemed not to be candidates for preoperative chemoradiation based on clinical staging, may be found to have more advanced disease at surgery, and may then require postoperative chemoradiation. Moreover, in patients with gastroesophageal junction carcinomas, the role of post-operative chemoradiation is supported by the phase III Intergroup trial (4). In this trial, 556 patients with gastric (around 80%) or gastroesophageal junction (around 20%)

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adenocarcinoma were randomized to receive either surgery alone or surgery with post-operative chemoradiation. Patients in the post-operative chemoradiation arm had a median survival of 36 months and patients in the surgery alone arm had a median survival of 27 months ($P=0.005$).

In summary, Jabbour et al. have presented a well-written, thorough, evidence-based review article on the role of postoperative chemoradiation and other approaches for the treatment of esophageal cancer. This review article will help increase our understanding of combined modality therapy for esophageal cancer.

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