Esophageal Cancer: Algorithm for Treatment According to Staging

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Esophageal cancer, though relatively uncommon in the United States, is a major global health threat. Squamous cell carcinoma remains the most common histology worldwide, whereas adenocarcinoma of the esophagus is increasing at epidemic proportions in the United States and other Western countries. But, in Korea, mortality rate of esophageal cancer is 2.4%, and the mortality/incidence ratio is 0.7. Squamous cell carcinoma remains the most common histology worldwide, whereas adenocarcinoma of the esophagus is increasing at epidemic proportions in the United States and other Western countries. Preoperative chemotherapy and combined preoperative chemoradiotherapy are also standards of treatment based on recent clinical trials. With the increasing use of chemotherapy as part of operative management as well, systemic chemotherapy will ultimately be used to treat the majority of patients with esophageal cancer.

The prognosis for patients with locally advanced esophageal cancer treated with the standard approaches of surgery or radiotherapy is poor. Treatment failure is due to both a high incidence of local-regional failure and early systemic dissemination of disease. Concurrent use of chemotherapy and radiotherapy is now a standard of care in the nonsurgical management of locally advanced esophageal cancer. According to NCCN Guideline Version 2.2012, the primary treatments of medically fit patients for devide into 2 groups; Preoperative chemoradiation, and definitive chemoradiation. And then, they recommend CT scan and PET/CT or PET for evaluation the response. In preoperative chemoradiation group, the outcomes of treatment devide into 3 groups; 1) no evidence of disease→ esophagectomy or observation, 2) persistence of local disease→ esophagectomy(preferred) or palliative therapy including chemotherapy 3) unresectable or metastasis→ palliative therapy. In definitive chemoradiation group, they recommend CT scan and PET/CT or PET for evaluation the response. In preoperative chemoradiation group, the outcomes of treatment devide into 3 groups; 1) no evidence of disease→ observe, 2) persistent local disease→ salvage esophagectomy, 3) new metastatic disease→ palliative therapy. In medically fit and locoregional disease, they recommend multidisciplinary evaluation- 1) Tis→ EMR or ablation 2) T1a→ esophagectomy or EMR, 3) T1b, No→ esophagectomy, 4) T1b N+→ esophagectomy for noncervical cancer, or chemoradiation for cervical cancer, 5) T2-4a, 4b→ primary treatment. In general, early studies of single-agent chemotherapy including bleomycin, 5-fluorouracil (5-FU) given by bolus or continuous infusion, cisplatin, and mitomycin evaluated only squamous cell carcinoma. Modest antitumor activity for a broad range of chemotherapy drugs is seen in esophageal carcinoma, but the duration of response to single-agent chemotherapy is generally brief and on the order of 4 to 6 months. In trials of patients with metastatic or unresectable disease, the response to cisplatin and 5-FU has been lower, ranging Cisplatin/5-FU has been accepted as a treatment standard in squamous cell and adenocarcinoma of the esophagus. More recent phase III trials have treated adenocarcinoma of the gastroesophageal junction in the context of gastric cancer studies; recent studies have also included squamous cell and adenocarcinoma of the esophagus in these trials - from 35% to 40%. The DCF regimen resulted in a higher response rate and longer time to progression (36%, 5.6 months) compared to 5-FU and cisplatin (26%, 3.7 months), but only a marginal median survival improvement (0.6 months) was noted for the three-drug regimen. Toxicity was substantial in both treatment arms, including hematologic and gastrointestinal toxicity,
with 82% of patients receiving the three-drug combination experiencing grade 3 or 4 neutropenia. The combination of irinotecan and infusional 5-FU was compared head to head to conventional 5-FU and cisplatin in a recent phase III trial in gastric and gastroesophageal junction cancers. There was no difference in response rate (26% vs. 32%), time to progression (4.2 vs. 5.0 months), or median survival (8.7 vs. 9.0 months). However, the toxicity profile significantly favored the irinotecan/5-FU combination, with less neutropenia, neutropenic fever, stomatitis, and nausea. There are few combination chemotherapy regimens in esophageal cancer that do not incorporate cisplatin. More recent non-cisplatin-containing combination trials have explored regimens including taxanes and irinotecan. Although these trials have indicated encouraging response rates in the phase II setting, substantial hematologic and gastrointestinal (diarrhea) toxicities of these regimens may not offer an advantage over the older cisplatin-containing regimens. Modest advances have been made in chemotherapy for esophageal cancer. A spectrum of single agents are active in esophageal cancer, including fluorinated pyrimidines, taxanes, platinum drugs, irinotecan, and mitomycin. Two-drug combinations modestly increase response rates, but translate into only a limited improvement in survival compared to single-agent therapy. The combination of 5-FU and cisplatin is widely used, and alternative two-drug regimens using either 5-FU or cisplatin as a backbone typically add either a taxane or irinotecan. Combined chemotherapy and radiation therapy are given preoperatively for esophageal adenocarcinoma and squamous cell carcinoma, and chemoradiotherapy without surgery is an accepted therapy standard for squamous cell cancer. Future research will focus on incorporating novel, molecularly targeted agents in the treatment of advanced disease and in the preoperative treatment of locally advanced disease.

References