En bloc esophagectomy reduces local recurrence and improves survival compared with transhiatal resection after neoadjuvant therapy for esophageal adenocarcinoma

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Objective: Neoadjuvant therapy is commonly used for esophageal adenocarcinoma. We have reported reduced local recurrence rates and improved survival after an en bloc esophagectomy compared with a transhiatal resection as primary therapy for adenocarcinoma of the esophagus. The aim of this study was to determine whether the benefits of an en bloc resection would extend to patients after neoadjuvant therapy.

Methods: The charts of all patients with esophageal adenocarcinoma that had neoadjuvant therapy and en bloc or transhiatal esophagectomy from 1992-2005 were reviewed. Patients found to have systemic metastatic disease at the time of the operation or who had an incomplete resection were excluded.

Results: There were 58 patients: 40 had an en bloc resection and 18 had a transhiatal esophagectomy. A complete pathologic response occurred in 17 (29.3%) of 58 patients. Median follow-up was 34.1 months after en bloc resection and 18.3 months after transhiatal resection (P = .18). Overall survival at 5 years and survival in patients with residual disease after neoadjuvant therapy was significantly better with an en bloc resection (overall survival: 51% for en bloc resection and 22% for transhiatal resection [P = .04]; survival with residual disease: 48% for en bloc resection and 9% for transhiatal resection [P = .02]). Survival in patients with complete pathologic response tended to be better after an en bloc resection (en bloc, 70%; transhiatal, 43%; P = .3).

Conclusion: An en bloc resection provides a survival advantage to patients after neoadjuvant therapy compared with a transhiatal resection, particularly for those with residual disease. Similar to patients treated with primary resection, an en bloc esophagectomy is the procedure of choice after neoadjuvant therapy.

he incidence of adenocarcinoma of the esophagus and esophagogastric junction is increasing faster than any other cancer in the Western world. Although survival is excellent in patients with early-stage tumors, unfortunately, most patients present with dysphagia and have locally advanced disease. The prognosis for these patients is poor, and consequently, attention has focused on the use of neoadjuvant therapy in an effort to reduce the local-regional tumor burden and eradicate micrometastatic systemic disease. During the past 2 decades, neoadjuvant chemoradiotherapy has been tested in numerous trials, and although a clear improvement in overall survival compared with that after surgical resection alone has not been demonstrated, subgroup analysis has suggested that patients who obtain a complete pathologic response have improved survival compared with those who have residual disease at the time of resection.² This finding has prompted some oncologists to recommend eliminating surgical resection after neoadjuvant therapy because it is thought that those with complete pathologic response do not need resection and those with incomplete response have such a poor prognosis that they are unlikely to benefit from the operation.

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Abbreviations and Acronyms

CT = computed tomography

PET = positron emission tomography

It has been our policy to reserve neoadjuvant therapy for patients with locally advanced disease based on findings from computed tomographic (CT) scans, endoscopic ultrasonographic analysis, and/or positron emission tomographic (PET) scanning. After neoadjuvant therapy, we have taken fit patients for an en bloc resection, given evidence that local recurrence is minimized and survival is maximized with this procedure in patients who have surgical intervention as the primary therapy for their cancer.³ The aim of this study was to review our experience and determine whether the local control and survival benefits of an en bloc esophagectomy would extend to patients after neoadjuvant therapy and in particular to those with residual disease on final pathology.

Materials and Methods Patient Population

The study population was drawn from all patients who had an esophagectomy for adenocarcinoma between 1993 and 2005 at the University of Southern California. Assessment of the extent of disease before surgical intervention included upper endoscopy, a chest and abdominal CT scan, and, when it became available, endoscopic ultrasonographic analysis (1997) and PET or CT–PET scanning (1998). Patients were considered to have advanced local-regional disease when there was evidence of multiple (>4) enlarged lymph nodes based on endoscopic ultrasonographic analysis. In patients who did not (unavailable) or could not (because of the size of the tumor) undergo endoscopic ultrasonography, a diagnosis of advanced local-regional disease was based on the endoscopic size and length of the tumor, CT scan evidence of a bulky tumor with or without enlarged peritumoral nodes, and/or PET scan findings consistent with multiple involved lymph nodes.

The records of all patients who had neoadjuvant therapy followed by an en bloc or a transhiatal esophagectomy for esophageal adenocarcinoma were reviewed. Neoadjuvant therapy was chemotherapy alone or chemoradiotherapy. Chemotherapy consisted of standard agents, including 5-fluorouracil, cisplatin, carboplatin, and/or paclitaxel. Patients were excluded if they were found to have systemic metastatic disease at the time of the operation, had a tumor that penetrated into an adjacent organ (T4), or had an incomplete pathologic resection (R1). In addition, patients who had an operation other than an en bloc or transhiatal esophagectomy were excluded. This study was approved by the Institutional Review Board of the University of Southern California.

En bloc esophagectomy was performed in patients who were younger than 75 years and who were free of substantial medical comorbidities. Transhiatal esophagectomy was performed in patients 75 years or older and those with significant cardiac or pulmonary disease or other major comorbid conditions. Patients were followed by the operating surgeon at regularly scheduled intervals (every 3 months for the first 3 years, every 6 months up to 5 years, and yearly

thereafter). CT scans of the chest and abdomen and routine blood chemistry results were obtained at each visit, and PET scans were obtained yearly.

Surgical Treatment

En bloc esophagectomy was performed as described in previous publications. 4 In brief, the en bloc dissection was performed through a right seventh-interspace posterolateral thoracotomy to have excellent exposure of the potentially involved mediastinal nodes below the carina, an upper midline laparotomy, and a left neck incision. The thoracic dissection removed en bloc the esophagus, azygos vein, thoracic duct, and surrounding lymph node-bearing mediastinal tissues. The borders of the dissection extend superiorly to above the azygos arch; laterally to include the left and right mediastinal parietal pleura; anteriorly to the membranous trachea, pericardium, and diaphragm; posteriorly to the spine and aorta; and inferiorly to the esophageal hiatus and down into the costal vertebral angle. Above the aortic arch, the dissection is kept adjacent to the esophagus to minimize potential injury to the recurrent laryngeal nerve. A paratracheal node dissection is not routinely performed for adenocarcinoma of the distal esophagus or gastroesophageal junction. The abdominal dissection was performed through an upper midline incision and removed the node-bearing tissue from the lateral surface of the right crus, the porta hepatis, and around the portal vein and the common hepatic, celiac, and left gastric arteries. Additionally, node-bearing tissue was removed from the lateral surface of the left crus, around the splenic artery, medial to the splenic hilum, and anterior to the adrenal gland. The en bloc dissection allowed systematic removal of lymph nodes in the following areas: low paratracheal, subcarinal, perihilar, paraesophageal, parahiatal, costalvertebral space, porta hepatis, superior retropancreatic, and around the portal vein and the hepatic, celiac, and splenic arteries.

Transhiatal dissection was performed as described by Orringer⁵ through an upper midline incision and a left neck incision. The lower mediastinal and esophageal dissection was performed through a widened diaphragmatic hiatus by using blunt and sharp dissection. Paraesophageal and mediastinal lymph nodes were removed as exposure allowed, but a complete node dissection in the mediastinum was not possible. The abdominal node dissection was identical to that described for the abdominal portion of the en bloc procedure.

Reconstruction in most patients was with a tubularized gastric pull-up, but if the stomach was unavailable or unsuitable, a colon interposition was performed. Reconstructions were preferentially placed in the posterior mediastinum, and the proximal anastomosis was hand sewn in the neck.

Statistical Analysis

Grouped data were expressed as medians with interquartile ranges. Statistical analysis appropriate for nonparametric data was used. Univariate analyses were performed by using the Fisher exact test for categorical variables and the Mann–Whitney test for continuous variables. Survival was calculated by using the Kaplan–Meier method, with comparisons of survival by means of the log-rank test.

Results

From January 1993 through August 2005, 416 patients with esophageal adenocarcinoma were seen by members of the

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