Comparison of endoscopic therapies and surgical resection in patients with early esophageal cancer: a population-based study

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Background: Outcome data comparing endoscopic eradication therapy (EET) and esophagectomy are limited in patients with early esophageal cancer (EC).

Objective: To compare overall survival and EC-related mortality in patients with early EC treated with EET and esophagectomy.

Design and Setting: Population-based study.

Patients: Patients with early EC (stages T0 and T1) were identified from the Surveillance, Epidemiology, and End Results database (1998-2009). Demographics, tumor specific data, and survival were compared. Cox proportional hazards regression models were used to evaluate the association between treatment and EC-specific mortality.

Intervention: EET and esophagectomy.

Main Outcome Measurements: Mid- (2 years) and long- (5 years) term overall survival and EC-specific mortality, outcomes based on histology and stage, treatment patterns, and predictors of cancer-specific mortality.

Results: A total of 430 (21%) and 1586 (79%) patients underwent EET and esophagectomy, respectively. There was no difference in the 2-year (EET: 10.5% vs esophagectomy: 12.7%, $P = .27$).and 5-year (EET: 36.7% vs esophagectomy: 42.8%, $P = .16$) EC-related mortality rates between the 2 groups. EET patients had higher mortality rates attributed to non-EC causes (5 years: 46.6% vs 20.6%, $P < .001$). Similar results were noted when comparisons were limited to patients with stage T0 and T1a disease and esophageal adenocarcinoma. There was no difference in EC-specific mortality in the EET compared with the surgery group (hazard ratio 1.4; 95% confidence interval, 0.9-2.03). Variables associated with mortality were older age, year of diagnosis, radiation therapy, higher stage, and esophageal squamous cell carcinoma.

Limitations: Comorbidities and recurrence rates were not available.

Conclusions: This population-based study demonstrates comparable mid- and long-term EC-related mortality in patients with early EC undergoing EET and surgical resection. (Gastrointest Endosc 2014;79:224-32.)

(footnotes appear on last page of article)

The incidence of esophageal cancer (EC) continues to increase faster than almost any other cancer in the Western World.[1,2] Despite the recent advances, patients with EC have a dismal 5-year survival rate of 16.8% (all stages).[3] Early EC, defined as disease limited to the mucosa or submucosa, constitutes approximately 20% of all cases of EC.[4,5] Given the high tumor-free survival rates, esophagectomy has been the standard treatment for patients with early EC, with which all other therapies are compared.[6-10] Esophagectomy in patients in whom the cancer has not yet penetrated the muscularis mucosa is associated with 5-year survival rates as high as 90%.[11] However, esophagectomy for early EC is associated with an overall operative mortality rate of 2% and major morbidity rate as high as 10%, even in high-volume centers and centers with multidisciplinary care.[11,12]

Based on a growing body of literature suggesting favorable outcomes compared with esophagectomy, endoscopic eradication therapies (EET) have gained gradual

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acceptance and are endorsed in society guidelines, especially in the field of Barrett's esophagus–related neoplasia.[4,9,12-16] The basic premise of EET is that patients with cancer limited to the mucosa have a very low risk (0-2%) of lymph node metastasis.[17] On the other hand, most experts agree that patients with submucosal, poorly differentiated cancer, size greater than 2 cm, and lymphatic or venous infiltration should generally be referred for surgical resection given the high risk of lymph node metastasis (at least 20%).[18] Although data suggest that EET are highly effective, studies comparing EET with surgical resection are limited.[4,9,10] Unfortunately, no randomized, controlled trial that can provide conclusive evidence of which of these 2 treatments is superior has been conducted nor are any such trials expected in the foreseeable future.

The aims of this study were to use the Surveillance, Epidemiology and End Results (SEER) database to (1) compare mid- (2 years) and long- (5 years) term overall survival and EC-specific mortality in patients with early EC treated with EET and esophagectomy, (2) compare outcomes (EC-free survival) based on histology (esophageal adenocarcinoms [EAC]) and stage, and (3) evaluate the treatment patterns and independent associations of treatment received with cancer-specific mortality.

METHODS

Data source

The SEER program is an ongoing contract-supported program of the National Cancer Institute to collect population-based cancer incidence, individual patient and tumor characteristics, initial treatment and follow-up survival data from U.S. cancer registries (http://www.seer.cancer.gov). Last expanded in 2010, SEER-18 includes 18 cancer registries that cover approximately 28% of the U.S. population.[19] Registries include the Alaska Natives, Metropolitan Atlanta, Greater California, Los Angeles, San Francisco-Oakland, San Jose-Monterey, as well as Connecticut, New Jersey, Detroit (Metropolitan), Iowa, Kentucky, Utah, Louisiana, New Mexico, Rural Georgia, Greater Georgia, Seattle (Puget Sound), and Hawaii. The SEER data contain deidentified patient data, and, therefore, this study was exempt from institutional review board review by the Office of Human Subject Research at the National Institutes of Health.

Study population

The study population comprised patients with a first primary EC (International Classification of Diseases for Oncology [ICD-O-3 codes]: C150-C155, C158-C159]), microscopically confirmed, and diagnosed from 1998 to 2009. All histologies were included. Patients diagnosed with early EC, as defined by the modified American Joint Committee on Cancer criteria, were included for analysis. SEER extent of disease codes were used to identify

Take-home Message

- Results of this population-based study demonstrate comparable 2- and 5-year esophageal cancer (EC)–specific survival rates between endoscopic eradication therapy (EET) and surgical resection in patients with early EC.
- Similar results were noted when analyses were limited to stage T0 and T1a disease and esophageal adenocarcinoma.
- Patients undergoing EET are more likely to die of other nonesophageal cancer–related causes.

patients with early EC (00, carcinoma in situ, invasive tumor confined to the mucosa [10], lamina propria [11], muscularis mucosae [12], and submucosa [16]). Patients with advanced stage disease (invasion of the muscularis propria and beyond (codes 20, 30, 40, 60, 65, 80, 85) or lymph node metastases); those who did not receive any EET or surgical treatment, coded as unknown for extension of tumor or metastasis (code 99); and those with a diagnosis only provided by death certificate were excluded.

Variable definitions

Demographic, treatment, and survival information were extracted. Early disease as defined by extent of disease variables was categorized as stage T0 (carcinoma in situ), stage T1a (invasive tumor confined to the mucosa, lamina propria, muscularis mucosae), or stage T1b (submucosa). Stage T1 encompasses both stage T1a and T1b disease. The SEER surgery codes used are similar to those based on the American College of Surgeons Commission on Cancer's Facility Oncology Registry Data System surgery codes, with supplementary annotations from the previous version of the SEER Program Code Manual (7). Surgery codes were categorized as endoscopic resection (with or without ablation therapy) or esophagectomy (partial or total). Variables analyzed also included age at diagnosis (year), sex, race (white, nonwhite), tumor histology (squamous cell carcinoma, adenocarcinoma, other), tumor stage (T0, T1a, T1b), tumor size, tumor grade (well, moderately, poorly, undifferentiated), radiation therapy (yes, no), SEER site (Northeast, Midwest, South, West), and year of diagnosis.

Statistical analyses

The frequencies and percentages of categorical variables and the means and standard deviations for continuous variables were calculated to characterize the treatment groups. Demographic features were compared between treatment groups by univariate analyses by using t tests for continuous variables and the χ^2 or Fisher exact test for categorical variables. For individuals with sufficient follow-up, we compared esophageal cancer-specific 2- and 5-year survival rates between EET and surgical resection.