Esophagectomy versus endoscopic resection for patients with early-stage esophageal adenocarcinoma: A National Cancer Database propensity-matched study

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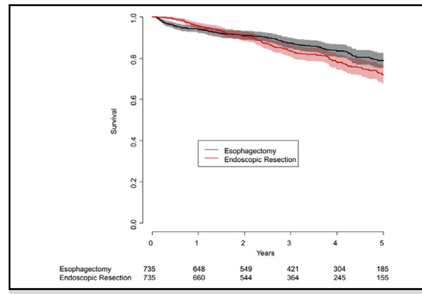
ABSTRACT

Objectives: Endoscopic resection has been rapidly adopted in the treatment of early-stage esophageal tumors. We compared the outcomes after esophagectomy or endoscopic resection for stage T1a adenocarcinoma.

Methods: We queried the National Cancer Database for patients with T1a esophageal adenocarcinoma who underwent esophagectomy or endoscopic resection and generated a balanced cohort with 735 matched pairs using propensity-score matching. We then performed a multivariable Cox regression analysis on the matched and unmatched cohorts.

Results: We identified 2173 patients; 1317 (60.6%) underwent esophagectomy, and 856 (39.4%) underwent endoscopic resection. In the unmatched cohort, patients who underwent esophagectomy were younger, more often not treated in academic settings, and more likely to have comorbidities (30.4% vs 22.5%, $P = .002$). They had longer hospital stays and more readmissions than patients who underwent endoscopic resection. Factors positively affecting overall survival were younger age, resection at an academic medical center, and lower Charlson–Deyo comorbidity score. In the matched cohort, patients who underwent esophagectomy had longer hospital stays and were more likely to be readmitted within 30 days (7.0% vs 0.6%, $P < .001$). When a time period–specific partition was applied, endoscopic resection had a lower death hazard 0 to 90 days after resection (hazard ratio, 0.15; $P = .003$), but this was reversed for survival greater than 90 days (hazard ratio, 1.34; $P = .02$).

Conclusions: In patients with early-stage esophageal adenocarcinoma, survival appears equivalent after endoscopic resection or esophagectomy, but endoscopic resection is associated with shorter hospital stays, fewer readmissions, and less 90-day mortality. In patients surviving more than 90 days, esophagectomy may provide better overall survival. (J Thorac Cardiovasc Surg 2018;■:1-8)



Survival of matched patients with T1a tumors after esophagectomy or endoscopic resection.

Central Message

Differences in survival were not seen after endoscopic resection or esophagectomy of stage T1a esophageal adenocarcinoma; endoscopic resection was associated with faster post-operative recovery.

Perspective

In a large database study, we did not find survival differences between patients who underwent endoscopic resection and patients who underwent esophagectomy. Patients who underwent an esophagectomy and survived more than 90 days appear to have better survival than patients who received endoscopic treatment, which may influence treatment planning for T1a tumors exhibiting characteristics linked with lymph node metastasis.

See Editorial Commentary page XXX.

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The incidence of esophageal adenocarcinoma has increased in recent decades.[1] Surveillance of Barrett's esophagus, a known precursor lesion that progresses to adenocarcinoma in 0.2% to 0.5% per patient-year, is associated with a diagnosis of esophageal adenocarcinoma at an earlier stage.[2-4] Early-stage esophageal cancer confined to the mucosa (T1a) has a low incidence of nodal metastases (5% in a

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Abbreviations and Acronyms

CDS	= Charlson–Deyo comorbidity score
IQR	= interquartile range
LVI	= lymph-vascular invasion
NCDB	= National Cancer Database
SEER	= Surveillance Epidemiology and End Results

recent meta-analysis) and can be treated by resection in most patients.[5-9] This corresponds to favorable 5-year survival, with rates as high as 77% to 100% for early-stage esophageal cancer.[5,10]

Endoscopic resection has been slowly replacing esophagectomy in the treatment of T1a esophageal adenocarcinoma.[11] Although the recurrence rate is higher after endoscopic resection when compared with esophagectomy (12% vs 7%), recurrent tumors often can be treated with endoscopic reexcision.[12,13] Previously reported retrospective series have not demonstrated differences in overall survival between esophagectomy and endoscopic resection in patients with early-stage esophageal cancer, but these studies had few patients in each group.[11,14,15]

The aim of the present study was to compare short-term outcomes and long-term survival in patients with T1a adenocarcinoma treated with esophagectomy or endoscopic resection using a large population-based database allowing for larger matched cohorts.

MATERIALS AND METHODS

Database and Patients

The National Cancer Database (NCDB) was queried for all patients with T1a esophageal adenocarcinoma who underwent esophagectomy or endoscopic resection from 2006 to 2012 and whose records contained complete pathology data. Patients who received preoperative chemotherapy or radiation therapy or had metastases at diagnosis were excluded. The 7th edition of the American Joint Committee on Cancer Union for International Cancer Control TNM staging was used. The patients were divided into 2 groups for analysis by treatment approach: esophagectomy and endoscopic resection. The NCDB data are completely de-identified; therefore, this study was reviewed by the Institutional Review Board of the University of Tennessee Health Science Center and deemed exempt from the requirements for informed consent.

Statistical Analysis

Patient characteristics are reported using mean ± standard deviation or median (interquartile range [IQR]) for continuous variables and frequencies and percentages for categoric variables. Pearson's chi-square test was used to compare categoric variables, and Student *t* test was used to compare continuous variables or their nonparametric alternatives.

To balance the clinical characteristics of the 2 treatment groups, we used propensity-score matching without replacement. We used a logistic regression model based on age, sex, race, insurance status, treatment facility type, Charlson–Deyo comorbidity score (CDS), tumor grade, and tumor size to estimate the propensity score. We used the recommended caliper width of 0.2 times the standard deviation of the logit of the propensity score.[16] Further, we used standardized differences to compare characteristics before and after the match using values less than 10 to indicate an acceptable balance (Figure E1).[17] We tested discrimination of the propensity model with the c-statistic and evaluated the overlap between groups using mirrored histograms (Figure E2).

Short-term outcomes of 30-day and 90-day mortality, 30-day readmission, and length of hospital stay were evaluated with chi-square and Wilcoxon rank sum because length of stay was not normally distributed. Long-term survival was analyzed by the Kaplan–Meier method. Survival analysis was performed using overall survival, defined as the time from diagnosis to death or censoring. In the matched cohort, we used the stratified results to account for the matched pairs. The Kaplan–Meier curves showed a violation of the proportional hazards assumption as the 2 curves crossed. To account for that violation, we partitioned the Kaplan–Meier analysis to examine short-term mortality (0-90 days) and long-term mortality (>90 days) by creating a time-dependent covariate.[18] Finally, we performed a univariable analysis and a multivariable Cox proportional hazards model in both our unmatched and matched cohorts. The variables included in these models were the time-dependent covariates described earlier: age, sex, treatment setting (academic or community), race, CDS, tumor grade, tumor size, and lymph-vascular invasion (LVI). The outcomes of these models are shown as hazard ratios and 95% confidence intervals. In the matched cohort, we stratified the Cox proportional hazards model by the matched pairs and used a robust variance estimator. Missing data for important variables were imputed using multiple imputation methods with sequential regression using the IVEWare software. SAS statistical software package version 9.4 (SAS Institute, Inc, Cary, NC) was used for the analysis.

RESULTS

Of 117,412 patients in the NCDB, we identified 2173 eligible patients with T1a esophageal adenocarcinoma; 1317 (60.6%) underwent esophagectomy and 856 (39.4%) underwent endoscopic resection (Table 1). Their mean age was 65.4 years, and the majority were male (1842/2173, 84.8%). Median follow-up time was 33 months for the endoscopic resection group and 49 months for the esophagectomy group.

Unmatched Comparisons

In the unmatched cohort, patients who underwent esophagectomy were younger, more often not treated in academic settings, and more likely to have a higher CDS (Table 1). Patients who underwent esophagectomy also had longer median hospital stay, more readmissions within 30 days, and higher 30-day and 90-day mortality (Table 2). The number of lymph nodes harvested was 12 (IQR, 6.0-19.0). Median survival was not achieved in this cohort, and 5-year survival estimates were 81.3% in patients who underwent esophagectomy and 70.9% in patients who underwent endoscopic resection (Figure 1). In both univariable and multivariable analyses of factors affecting survival, younger age, resection at an academic institution, and lower CDS were associated with better survival (Tables 3 and 4). Endoscopic resection positively affected survival during the first 90 days after resection, whereas esophagectomy was associated with better survival after 90 days (Tables 3 and 4).