HHS Public Access
Author manuscript
Gastrointest Endosc. Author manuscript; available in PMC 2017 August 01.

Published in final edited form as:
Gastrointest Endosc. 2016 August ; 84(2): 232–240.e1. doi:10.1016/j.gie.2016.01.019.

Outcomes after endoscopic versus surgical therapy for early esophageal cancers in an older population

Linda C. Cummings, MD, MS[1,2], **Tzuyung Doug Kou, PhD**[2], **Mark D. Schluchter, PhD**[2], **Amitabh Chak, MD**[1,2], and **Gregory S. Cooper, MD**[1,2]

[1]Division of Gastroenterology and Liver Disease, Department of Medicine, University Hospitals Case Medical Center, Cleveland, Ohio

[2]Case Western Reserve University, Cleveland, Ohio

Abstract

Background and Aims—Endoscopic treatment of early esophageal cancer provides an alternative to esophagectomy, which older patients may not tolerate. Population-based data regarding short-term outcomes and recurrence after endoscopic treatment for esophageal cancer are limited. We compared short-term outcomes, treated recurrence, and survival after endoscopic versus surgical therapy for early esophageal cancers in an older population.

Methods—We conducted a retrospective cohort study identifying patients aged ≥66 years with Tis or T1a tumors without nodal involvement diagnosed from 1994 to 2011 from the linked Surveillance, Epidemiology and End Results (SEER)-Medicare database.

Results—Out of 2193 patients, 41% (n = 893) underwent esophagectomy and 12% (n = 255) underwent endoscopic treatment within 6 months of diagnosis. Those treated endoscopically were older and more likely to have a Charlson comorbidity score ≥2. A composite endpoint, hospitalization and/or adverse events at 60 days, was higher in surgical patients than the endoscopic treatment group (30% vs. 12%, p<0.001). In a Cox model stratified by histology, adjusting for other factors, endoscopic treatment was associated with an improved 2-year survival (hazard ratio [HR], 0.51; 95% CI, 0.36 – 0.73)

Conclusions—In this older population, a composite short-term endpoint was worse in the surgical group. Endoscopic treatment was associated with improved survival through 2 years. These results suggest that endoscopic treatment is a reasonable approach for early esophageal cancers in the elderly.

Corresponding Author: Dr. Linda C. Cummings, University Hospitals Case Medical Center, 11100 Euclid Avenue, Cleveland, OH 44106-5066. linda.cummings@case.edu; Phone: (216) 844-3217.

Specific author contributions: Linda C. Cummings: conception and design of the study, funding, IRB, statistical analysis, interpretation of results, and manuscript preparation; Tzuyung Doug Kou: computer analysis, statistical analysis, and manuscript preparation; Mark Schluchter: study design, statistical analysis, interpretation of results, and manuscript preparation; Amitabh Chak: study design, interpretation of results, and manuscript preparation; Gregory S. Cooper: study design, interpretation of results, and manuscript preparation. All authors have approved the final draft submitted.

Introduction

Esophageal cancer carries a poor prognosis, with a 40% 5-year survival rate for localized disease.[1] In the United States, this cancer predominantly affects older individuals, with a median age at diagnosis of 67.[2] Although esophagectomy provides the best chance of cure for early Stage I esophageal cancer (T1N0M0) and high-grade dysplasia (TisN0M0), it is a technically demanding, invasive operation with potentially high rates of short-term mortality (7%–13%)[3] and morbidity. In elderly patients who often have comorbid conditions, short-term risks may outweigh the benefit of long-term cure offered by esophagectomy. Endoscopic treatment (ET) with resection, often performed with ablation, is gaining acceptance and may be better tolerated in elderly patients. Endoscopic treatment can particularly be used for high-grade dysplasia and superficial cancers confined to the lamina propria or muscularis mucosae (T1a) due to low likelihood of lymph node metastasis.[4] Endoscopic methods may, however, raise concerns about inadequate resection because they yield markedly limited tissue specimens compared with esophagectomy. Assessment of tumor depth of invasion and nodal involvement by EUS may guide treatment approach.[5]

Previous research assessing esophagectomy in older patients has not compared its effectiveness with endoscopic treatment. We therefore aimed to compare short-term and long-term outcomes among older patients undergoing endoscopic treatment versus esophagectomy. We hypothesized that endoscopic treatment of early esophageal cancer provides comparable long-term outcomes and favorable short-term outcomes compared with esophagectomy in elderly patients. Our primary outcome was 2-year survival. Other outcomes of interest included hospitalizations, adverse events, and death at 60 days; need for dilation; and use of EUS.

Methods

We performed a retrospective cohort study using the Surveillance, Epidemiology and End Results (SEER) tumor registry data linked to Medicare claims (SEER-Medicare) to identify patients with early esophageal cancer or high-grade dysplasia. The study protocol was approved by the University Hospitals Case Medical Center Institutional Review Board and the National Cancer Institute (NCI).

Data Sources

NCI's SEER program provides reliable data regarding cancer incidence from cancer registries which, after its latest expansion in 2010, now covers approximately 28% of the U.S. population.[6] SEER collects data regarding patients with a confirmed cancer diagnosis including demographic information, presenting stage, lymph node involvement, histology, surgery and radiation treatment within 4 months of diagnosis, and survival. Linkage of SEER to Medicare claims data allows identification of comorbidities and treatment beyond the first 4 months after cancer diagnosis. Procedures can be identified in SEER and from Medicare hospital inpatient claims (MedPAR), physician-supplier claims (National Claims History, NCH), or Standard Analytical File (SAF) outpatient claims. Procedures in MedPAR are identified through International Classification of Diseases, 9th revision-clinical modification (ICD-9-CM) procedure codes. Procedures from NCH and SAF are identified through Current Procedural Terminology (CPT) codes.

Study Population

Patients with incident cases of high-grade dysplasia or early esophageal cancer diagnosed between 1994 and 2011 who underwent esophagectomy or endoscopic treatment within 6 months of diagnosis were identified. In order to capture comorbid conditions and outpatient procedures, patients had to participate in Medicare Part A and B from 6 months before diagnosis until 9 months after diagnosis or death. Patients aged ≥66 at diagnosis were included to assess comorbid conditions and to evaluate use of EUS before cancer diagnosis. We excluded patients enrolled in a Health Maintenance Organization (HMO) from 6 months before to 3 months after cancer diagnosis, due to incomplete claims data; patients not enrolled in Medicare Part B, due to lack of outpatient claims data; and patients with prior cancer.

Measures

Patient, Hospital, and Tumor Characteristics—Patient demographic characteristics including age, race, marital status, SEER registry, and gender were obtained from SEER. Cases with anatomical site recorded as esophagus were included. Histology as reported by ICD-O-3 coding was classified as adenocarcinoma or squamous cell carcinoma according to the Collaborative Stage Data Collection System Version 02.04.[7] Cases with tumor depth classified as in situ (Tis) or extending into the mucosa (T1a) were included based on SEER variables for tumor extension (e10ex1 for cases diagnosed 1994–2003, coded as 00 or 10–12 and csex1 for cases diagnosed 2004–2011, coded as 000, 100, 110, or 120). Cases with T1b and greater tumor depth, lymph node involvement, or metastatic disease at presentation were excluded.

Geographic Characteristics—County-level Area Health Resources Files (AHRF) data regarding education (% residents with a college education) and median income were used as proxy for socioeconomic status. County-level gastroenterologist and primary care provider density per 1000 population were characterized using AHRF data. Cases missing AHRF data were excluded. AHRF data were categorized into quartiles due to their skewed distribution. SEER registries were grouped into 4 geographic regions (Northeast, Midwest, South, and West).

Comorbidities—A modified version of the Deyo adaptation of the Charlson comorbidity index was used to identify comorbid conditions using ICD-9-CM diagnosis codes from inpatient, outpatient, and physician-supplier claims.[8] Malignancy was excluded from the Charlson calculation.

Treatment Approach—Patients with early esophageal cancer undergoing esophagectomy or endoscopic treatment (ablation, local tumor destruction, or endoscopic mucosal resection) from 1 month before 6 months after diagnosis were included. Because use of both SEER (which records the most invasive cancer-directed treatment) and Medicare claims may enhance identification of cancer surgery,[9] patients receiving endoscopic treatment according to SEER with no Medicare claims for esophagectomy 1 month before 6 months after cancer diagnosis were classified in the endoscopic treatment group. Treatment approach was also identified from Medicare inpatient, outpatient, and physician-supplier claims. Patients undergoing both endoscopic treatment and esophagectomy within 6 months of diagnosis were included in the esophagectomy group. Procedure codes used to identify treatment approach (Supplementary Table 1) include ones suggested by the ASGE Technology Committee to be the most applicable for endoscopic treatment.[10] Radiation therapy as first course of treatment was assessed through SEER (variable rad1) and demonstrated high concordance (κ statistic = 0.802) with receipt of radiation in Medicare claims as identified through a previously published algorithm.[11]

EUS—Receipt of EUS was assessed within 30 days before diagnosis to 3 months after diagnosis as in a previous study from our group.[12] EUS was identified from outpatient and physician-supplier files with the following CPT codes: 43231, 43232, 43242, 43259, 76975.

Short-term Outcomes—Hospital admission was defined as admission to an acute care hospital within 60 days of discharge after hospitalization (for esophagectomy) or procedure (for endoscopic treatment). Admissions to skilled nursing care, rehabilitation facilities, and long-term care hospitals were excluded. Adverse events within 60 days identified from inpatient, outpatient, and physician-supplier claims included post-procedural interventions; as previously suggested,[13] they are closely associated with severe adverse events. Adverse events were identified using the following ICD-9-CM diagnosis codes and procedure codes (ICD-9-CM and CPT): hemorrhage complicating a procedure (998.1), accidental puncture or laceration during a procedure (998.2), retrieval of retained foreign body (CPT 49085; ICD-9 54.92), management of postoperative shock/hemorrhage (ICD-9 39.98), management of abdominal infection (CPT 49020, 49021, 49040, 49041, 49060, 49061, 49080, 49081, 75989; ICD-9 54.0, 54.91, 54.19), repair of an organ injury/laceration (CPT 38100, 44602, 44603; ICD-9 31.71, 33.41, 41.5, 42.82, 44.61, 46.71, 46.73, 50.61, 51.91), reoperative laparotomy (CPT 49002, 49000, 49010; ICD-9 54.12, 54.11, 54.21), management of wound adverse event (CPT 10060, 10061, 10120, 10121, 10140, 10180, 12020, 13160, 97601, 97602; ICD-9 54.61, 86.22), and management of bowel obstruction (CPT 44050). An a priori composite short-term outcome measure, defined as hospitalization and/or adverse event within 60 days, was evaluated to comply with NCI policy which bars reporting of events with frequency <11. Perioperative mortality was defined as death occurring within 60 days of esophagectomy or endoscopic treatment.

Dilation—Endoscopic dilation within 6 months of esophagectomy or endoscopic treatment was evaluated from inpatient, outpatient, and physician-supplier files. The following codes were used to identify dilation: CPT 43220, 43249, 43226, 43248, 43450, 43453, 43456; ICD-9 42.92.

Treated Recurrence—Similar to a previously published algorithm for identifying cancer relapse,[14] treatment for recurrent disease was assessed by receipt of chemotherapy and/or radiation >6 months after endoscopic or surgical treatment. Receipt of chemotherapy was identified from MedPAR, physician-supplier, and SAF files with the following codes:

chemotherapy administration (99.25), antineoplastic chemotherapy encounter (V58.11), cancer chemotherapy follow-up (V67.2), convalescence and palliative care after chemotherapy (V66.2), outpatient or physician administration of chemotherapy (Q0083 – Q0085), chemotherapeutic agents (Healthcare Common Procedure Coding System codes J9000 – J9999), and revenue center codes (0331, 0332, 0335). Radiation therapy was identified with ICD-9 codes 92.2, V58.0, V66.1, and V67.1, CPT codes 77xxx, and revenue center codes 0330 and 0333. The proportion of patients receiving endoscopic treatment within the first 6 months of diagnosis who subsequently underwent esophagectomy was assessed.

Statistical Analysis

Pearson's chi-square test or Fisher's exact test was used to compare categorical variables among treatment groups. Continuous variables were compared using parametric or nonparametric tests as appropriate. Survival was measured from cancer diagnosis to death or last follow-up through December 31, 2013. Kaplan-Meier curves were generated to compare survival between treatment groups; the log-rank test was used to compare survival curves. Cox proportional hazards models were used to evaluate treatment approach and other covariates and their association with survival time. Due to the known association between histology and long-term survival, our primary analysis was a Cox model stratified by histology. We included all tracked covariates in multivariable models as they were felt to be clinically meaningful. Potential proportional hazards assumption violations were assessed by testing for the interaction of covariates with time and through visual inspection of Kaplan-Meier curves and log[-log(survival)] versus survival time plots. For 2-year survival analysis, patients' survival times were censored at 2 years. To assess effects of perioperative mortality or timing of diagnosis on long-term survival, multivariable Cox models stratified by histology censoring patients dying within 60 days of the procedure or limiting the cohort to patients diagnosed from 2002 to 2009 were developed. Data were analyzed using SAS software version 9.3 (Cary, NC). As a secondary analysis, a propensity score (PS) model was used to adjust for potential selection bias because of nonrandom treatment allocation. Propensity scores, the predicted probability of receiving endoscopic treatment,[15] were generated through non-parsimonious logistic regression models incorporating all observed covariates evaluated in the multivariable Cox proportional hazards models. Endoscopic treatment and esophagectomy patients were matched 1:1 by propensity scores using a previously described matching algorithm.[16]

Results

From SEER-Medicare data, we identified 38,519 patients with esophageal cancer, including 2,193 patients with early stage esophageal cancer (Tis, T1a) who met our inclusion and exclusion criteria. Figure 1 displays stepwise cohort identification. Among 2193 patients, 41% (n = 893) primarily underwent esophagectomy and 12% (n = 255) underwent endoscopic treatment within 6 months of diagnosis. Of the remaining 1,045 patients who did not receive either treatment, 58% (n = 610) received radiation therapy as a first course of treatment. The mean follow-up time was 3.5 years (standard deviation [SD], 3.6 years) and was longer among patients undergoing esophagectomy (5.0 years, SD 4.1 years) or endoscopic treatment (4.3 years, SD 2.4 years).

Baseline demographic characteristics by treatment approach are presented in Table 1. Patients who did not receive esophagectomy or endoscopic treatment were more likely to be non-white and more likely to receive radiation than patients who were treated with esophagectomy or endoscopic treatment. Among patients receiving endoscopic or surgical treatment, there were no significant differences with respect to gender, racial makeup, histology, SEER registry, county-level physician density, or county-level education and income. However, endoscopically treated patients were older than those undergoing esophagectomy and were more likely to have Tis tumors and Charlson score ≥2. Within the esophagectomy and endoscopic treatment groups, among those receiving radiation (19% and 14%, respectively), the vast majority (>94%) had T1a tumors. Over the study period, the rate of endoscopic treatment increased over time, with 91% of endoscopic cases occurring in 2002 or later. Use of EUS varied among treatment groups; only 17% (n=182) of patients not receiving esophagectomy or endoscopic treatment underwent EUS, compared with 41% (n = 367) of esophagectomy patients and 59% (n = 151) of endoscopically treated patients.

Short-Term Outcomes and Treated Recurrence

A composite endpoint of hospitalization and/or adverse events at 60 days after the procedure was significantly higher in the esophagectomy group (30%, n = 265) than the endoscopic treatment group (12%, n = 30; $p<0.001$). The rate of dilation was higher in the esophagectomy group (25%, n = 220) than the endoscopic treatment group (15%, n = 39; $p<0.01$). The rate of death at 60 days was significantly higher in the esophagectomy group (4%) than the endoscopic treatment group (numbers suppressed due to counts <11). There was no difference in the rate of treated recurrence in the esophagectomy group (16%, n=139) and the endoscopic treatment group (13%, n=32; $p=0.23$). Among patients treated endoscopically, 15 subsequently underwent esophagectomy >6 months after cancer diagnosis.

Overall Long-Term Survival

Kaplan-Meier curves showing overall survival by treatment approach up to 2 years after diagnosis are shown in Figure 2. There were significant differences in unadjusted 2-year survival by treatment approach ($p<0.001$ by log-rank test). 2-year unadjusted survival was 71% in the esophagectomy group and 84% in the endoscopic treatment group among adenocarcinoma patients compared with 60% and 76%, respectively, among squamous cell carcinoma patients. The results of the Cox model stratifying by histology adjusted for other factors are presented in Table 2. Endoscopic treatment was associated with decreased mortality (HR, 0.51; 95% CI, 0.36 – 0.73). Increasing age and receipt of radiation were independent predictors of mortality. Cases diagnosed from 2002 to 2009 and Tis lesions were associated with a decreased risk of death.

We conducted several sensitivity analyses to assess the robustness of our results. A Cox model censoring patients dying within 60 days of the procedure developed to evaluate the impact of perioperative mortality on long-term survival demonstrated that endoscopic treatment was associated with decreased mortality through 2 years after adjusting for other factors (HR, 0.61; 95% CI, 0.45 – 0.85). Among patients matched 1:1 by treatment approach based on propensity scores, endoscopic treatment remained associated with decreased mortality (HR, 0.59; 95% CI, 0.41 – 0.86). Among patients diagnosed between 2002 and 2009 (a time period accounting for most endoscopically treated cases), endoscopic treatment was associated with decreased mortality (HR, 0.51; 95% CI, 0.36 – 0.74) after adjusting for other factors.

Discussion

The current study compared short-term and long-term outcomes in elderly patients undergoing treatment for early esophageal cancer. We demonstrated favorable short-term and long-term outcomes in patients undergoing endoscopic treatment compared with surgical resection. Previous studies evaluating the morbidity and mortality associated with esophageal cancer resection among elderly patients used varying age cutpoints between 65 and 75.[17–20] Some data have demonstrated increased risk of cardiopulmonary adverse events in older patients after esophagectomy, but no difference in operative or long-term mortality compared with younger patients.[17, 18] In contrast, one study reported an 11% 30-day mortality rate after esophagectomy in a Medicare population compared with 4% to 7% in younger cohorts.[20] A study of patients aged ≥70 undergoing esophagectomy for esophageal cancer (predominantly adenocarcinoma) reported a 5-year survival rate of 24%.[17] A recent single center study found no increase in adverse events in patients aged ≥75 undergoing endoscopic mucosal resection for Barrett's esophagus lesions compared with younger patients.[21]

In our study, only 52% of 2193 patients with early disease underwent esophagectomy or endoscopic treatment within the first 6 months. The proportion of non-white patients was higher among patients not receiving esophagectomy or endoscopic treatment (Table 1). This finding may reflect the lower proportion of adenocarcinomas (which typically affect white patients) among this group, although previous studies have demonstrated underuse of surgery among potentially resectable patients with esophageal cancer, particularly in non-white patients.[22, 23]

In the current study, among patients not receiving esophagectomy or endoscopic treatment, 58% (n=610) received radiation therapy as a first course of treatment. However, radiation therapy is not part of the treatment algorithm in the National Comprehensive Cancer Network (NCCN) guidelines for node-negative cancers with Tis or T1a disease.[24] Presumably these patients were not deemed surgical candidates, were not offered endoscopic treatment, or declined surgery. Patients in this group were more likely to have Charlson score ≥2 (10%, n=109) than those in the endoscopic treatment and surgery groups. Among patients receiving endoscopic or surgical treatment, radiation therapy was independently associated with increased mortality. This finding is consistent with previous analyses not focused on the elderly comparing endoscopic and surgical treatment for early esophageal cancers.[25–27]

The unadjusted 2-year survival among adenocarcinoma patients in the current study was 71% in the esophagectomy group and 84% in the endoscopic treatment group. Direct comparison with other studies is challenging due to differences in setting, patient selection, and outcome measurement. Our results compare favorably to previous SEER-Medicare analyses reporting 53% to 57% 1-year survival after esophagectomy for locoregional cancer; however, one of those studies measured survival from the date of surgery rather than date of cancer diagnosis.[3, 28] On the other hand, 5-year survival after esophagectomy for Stage I esophageal adenocarcinoma has been reported to be as high as 81% to 95% in tertiary center case series.[29–31]

As in other studies,[25–27, 32] we found that increasing age was an independent predictor of mortality. Although Steyerberg et al[32] found that increasing comorbidity was associated with increased risk of death, Charlson score ≥2 was not an independent predictor of mortality in our stratified Cox model through 2 years. In our study, endoscopic treatment was associated with better survival through 2 years. This finding could reflect better tolerability of this less-invasive procedure or the lower proportion of T1a lesions. Perioperative mortality does not explain improved long-term survival in the endoscopic treatment group because survival analysis censoring patients who died perioperatively still demonstrated decreased mortality with endoscopic treatment. Beyond the first 2 years after cancer diagnosis, endoscopically treated patients may have been more likely to die from non cancer-related causes especially considering they were more likely to have Charlson score ≥2. Our selection of 2-year survival as an outcome encompassed a time period after diagnosis during which many recurrences would probably have been captured.[33]

The overall rate of EUS was 32%, or 700 of 2193 patients in our cohort. EUS was more frequently performed in patients receiving esophagectomy (41%) and endoscopic treatment (59%). In previous SEER-Medicare studies which also included patients with more advanced stage, only 16% to 21% of patients undergoing esophagectomy and 12% to 22% of patients with in situ or localized disease underwent EUS.[12, 34] However, the rate of EUS among patients with early disease undergoing esophagectomy was not reported. Although accuracy of EUS in early esophageal cancers has been debated, with some proposing that endoscopic resection should be used as a primary staging modality,[35] a more recent meta-analysis demonstrated that EUS had 85% sensitivity and 87% specificity for staging T1a tumors compared with final staging by endoscopic mucosal resection or surgical resection.[5]

We found that short-term outcomes including dilation, a composite endpoint of hospitalizations and/or adverse events at 60 days, and perioperative deaths were significantly higher in the esophagectomy group. We examined short-term mortality at 60 days because 30-day mortality may not provide a complete assessment after esophagectomy.[36] We assessed dilation within 6 months of treatment as these procedures would likely reflect treatment of dysphagia secondary to anatomotic or post-endoscopic resection stricture rather than palliation of recurrent malignant disease. Hospitalizations, adverse events, and dilation potentially impact health-related quality of life; indeed, major postoperative adverse events have been shown to have a long-term impact on health-related quality of life after esophagectomy.[37] Our results suggest that, over the short term, esophagectomy for early esophageal cancer in elderly patients is associated with greater morbidity and potentially greater mortality.

Our study is unique in several respects. Although other studies have compared long-term outcomes after endoscopic treatment versus surgery, they have not focused on elderly patients, in whom surgical risks are potentially greater. Our study is unusual in its evaluation of short-term outcomes at a population level. We also assessed use of EUS and dilation in this population. Because SEER captures approximately one fourth of the U.S. population, our results can likely be generalized to the elderly.

Despite its strengths, the study had several limitations. Claims data lack detailed clinical information and do not capture patient preferences or patient characteristics such as frailty which may impact decision-making regarding treatment approach. Most likely, not all endoscopically treated cases were identified because endoscopic mucosal resection lacks unique ICD-9-CM procedure codes or CPT codes. Due in part to NCI's data confidentiality policy, we were unable to adjust for esophagectomy volume, which may have impacted mortality. Adverse events were likely undercoded; we focused on temporally correlated adverse events requiring intervention, as these may be more likely to occur in administrative data.[13] Nonetheless, because codes used to identify adverse events were not specific to endoscopy or esophagectomy, without access to medical records we cannot definitively ascribe these codes to treatment approach. Finally, our ability to detect differences in outcomes between treatment groups was limited by the relatively small number of patients receiving endoscopic treatment within each histology.

In summary, in this elderly population, esophagectomy for early esophageal cancer was associated with worse short-term and long-term outcomes. Based on our results, endoscopic treatment may be a preferred approach for early esophageal cancers in the elderly. Future studies could compare health-related quality of life in older patients undergoing endoscopic versus surgical treatment for early esophageal cancers or evaluate costs associated with these treatment strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database. Preliminary results from this study using older data were presented at DDW 2014 (published in Gastroenterology 2014;146(5S):661).

Financial support: This study was funded by Grant #IRG-91-022-18 to the Case Comprehensive Cancer Center from the American Cancer Society, awarded to L.C. Cummings. L.C.C. was supported by NIH grant P50 CA150964 (Case Western Reserve University GI SPORE) and American College of Gastroenterology Junior Faculty Development Award. A.C. was supported by NIH grants U54CA163060 (Case Barrett's Esophagus Translational Research Network) and P50 CA150964 (Case GI SPORE). G.S.C. was supported by NIH grant P50 CA150964 (Case GI SPORE), UL1 TR000439 (Case Clinical & Translational Science Collaborative), and P30 CA043703 (Case Comprehensive Cancer Center).

Glossary

AHRF	Area Health Resources Files
CI	Confidence interval
CPT	Current Procedural Terminology
ET	Endoscopic treatment
EUS	Endoscopic ultrasound
HMO	Health Maintenance Organization
HR	Hazard Ratio
ICD-9-CM	International Classification of Diseases, 9th revision-clinical modification
NCCN	National Comprehensive Cancer Network
NCH	National Claims History
NCI	National Cancer Institute
PS	Propensity score
Q	Quartile
SAF	Standard Analytical File
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
SEER	Surveillance, Epidemiology and End Results

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA: Cancer J Clin. 2015; 65(1):5–29. [PubMed: 25559415]
2. [accessed 10/18/15] SEER Cancer Statistics Factsheets: Esophageal Cancer. http://seer.cancer.gov/statfacts/html/esoph.html
3. Chang AC, Ji H, Birkmeyer NJ, Orringer MB, Birkmeyer JD. Outcomes After Transhiatal and Transthoracic Esophagectomy for Cancer. The Annals of Thoracic Surgery. 2008; 85(2):424–9. [PubMed: 18222237]
4. Stein HJMDF, Feith MMD, Bruecher BLDMMD, Naehrig JMD, Sarbia MMD, Siewert JRMDF. Early Esophageal Cancer: Pattern of Lymphatic Spread and Prognostic Factors for Long-Term Survival After Surgical Resection. Annals of Surgery. 2005; 242:260–9. [PubMed: 16041217]
5. Thosani N, Singh H, Kapadia A, et al. Diagnostic accuracy of EUS in differentiating mucosal versus submucosal invasion of superficial esophageal cancers: a systematic review and meta-analysis. Gastrointestinal Endoscopy. 2012; 75(2):242–53. [PubMed: 22115605]
6. [accessed 04/03/2014] Surveillance, Epidemiology, and End Results Database. http://seer.cancer.gov
7. [accessed 10/28/13] Collaborative Stage for TNM 7, Esophagus Histologies Stage Table. http://web2.facs.org/cstage0204/esophagus/Esophagus_xhw.html

8. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. Journal of Clinical Epidemiology. 1992; 45:613–9. [PubMed: 1607900]
9. Cooper GS, Virnig B, Klabunde CN, Schussler N, Freeman J, Warren JL. Use of SEER-Medicare Data for Measuring Cancer Surgery. Medical Care. 2002; 40(8):IV-43–IV-8.
10. Kantsevoy SV, Adler DG, Conway JD, et al. Endoscopic mucosal resection and endoscopic submucosal dissection. Gastrointestinal Endoscopy. 2008; 68(1):11–8. [PubMed: 18577472]
11. Abrams JA, Buono DL, Strauss J, McBride RB, Hershman DL, Neugut AI. Esophagectomy compared with chemoradiation for early stage esophageal cancer in the elderly. Cancer. 2009; 115(21):4924–33. [PubMed: 19637343]
12. Das A, Chak A, Sivak M, Payes J, Cooper G. Endoscopic ultrasonography and prognosis of esophageal cancer. Clinical Gastroenterology and Hepatology. 2006; 4:695–700. [PubMed: 16713744]
13. Billingsley KG, Morris AM, Dominitz JA, et al. Surgeon and hospital characteristics as predictors of major adverse outcomes following colon cancer surgery: Understanding the volume-outcome relationship. Archives of Surgery. 2007; 142(1):23–31. [PubMed: 17224497]
14. Earle CC, Nattinger AB, Potosky AL, et al. Identifying Cancer Relapse Using SEER-Medicare Data. Medical Care. 2002; 40(8):IV-75–IV-81.
15. Austin P, Mamdani M, Stukel T, Anderson G, Tu J. The use of the propensity score for estimating treatment effects: administrative versus clinical data. Statistics in Medicine. 2005; 24:1563–78. [PubMed: 15706581]
16. Parsons, LS. [accessed 07/13/2015] Performing a 1:N Case-Control Match on Propensity Score. SUGI 29 Proceedings. 2004. http://www2.sas.com/proceedings/sugi29/165-29.pdf
17. Alexiou C, Beggs D, Salama FD, Brackenbury ET, Morgan WE. Surgery for esophageal cancer in elderly patients: The view from Nottingham. The Journal of Thoracic and Cardiovascular Surgery. 1998; 116(4):545–53. [PubMed: 9766581]
18. Fang W, Igaki H, Tachimori Y, Sato H, Daiko H, Kato H. Three-field lymph node dissection for esophageal cancer in elderly patients over 70 years of age. The Annals of Thoracic Surgery. 2001; 72(3):867–71. [PubMed: 11565672]
19. Internullo E, Moons J, Nafteux P, et al. Outcome after esophagectomy for cancer of the esophagus and GEJ in patients aged over 75 years. European Journal of Cardio-Thoracic Surgery. 2008; 33(6):1096–104. [PubMed: 18407509]
20. Steyerberg EW, Neville BA, Koppert LB, et al. Surgical Mortality in Patients With Esophageal Cancer: Development and Validation of a Simple Risk Score. Journal of Clinical Oncology. 2006; 24(26):4277–84. [PubMed: 16963730]
21. Qumseya B, David W, Woodward TA, et al. Safety of esophageal EMR in elderly patients. Gastrointestinal Endoscopy. 2014; 80(4):586–91. [PubMed: 24703086]
22. Paulson EC, Ra J, Armstrong K, Wirtalla C, Spitz F, Kelz RR. Underuse of Esophagectomy as Treatment for Resectable Esophageal Cancer. Arch Surg. 2008; 143(12):1198–203. [PubMed: 19075172]
23. Dubecz A, Sepesi B, Salvador R, et al. Surgical Resection for Locoregional Esophageal Cancer Is Underutilized in the United States. Journal of the American College of Surgeons. 2010; 211(6): 754–61. [PubMed: 20980174]
24. [accessed 2/7/15] National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers. http://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf
25. Das A, Singh V, Fleischer DE, Sharma VK. A Comparison of Endoscopic Treatment and Surgery in Early Esophageal Cancer: An Analysis of Surveillance Epidemiology and End Results Data. Am J Gastroenterol. 2008; 103(6):1340–5. [PubMed: 18510606]
26. Ngamruengphong S, Wolfsen HC, Wallace MB. Survival of Patients With Superficial Esophageal Adenocarcinoma After Endoscopic Treatment vs Surgery. Clinical Gastroenterology and Hepatology. 2013; 11(11):1424–9. [PubMed: 23735443]
27. Wani S, Drahos J, Cook MB, et al. Comparison of endoscopic therapies and surgical resection in patients with early esophageal cancer: a population-based study. Gastrointestinal Endoscopy. 2014; 79(2):224–32. [PubMed: 24060519]

28. Smith GL, Smith BD, Buchholz TA, et al. Patterns of Care and Locoregional Treatment Outcomes in Older Esophageal Cancer Patients: The SEER-Medicare Cohort. International journal of radiation oncology, biology, physics. 2009; 74(2):482–9.

29. Portale G, Hagen JA, Peters JH, et al. Modern 5-Year Survival of Resectable Esophageal Adenocarcinoma: Single Institution Experience with 263 Patients. Journal of the American College of Surgeons. 2006; 202(4):588–96. [PubMed: 16571425]

30. Pech O, Bollschweiler E, Manner H, Leers J, Ell C, Hölscher AH. Comparison Between Endoscopic and Surgical Resection of Mucosal Esophageal Adenocarcinoma in Barrett's Esophagus At Two High-Volume Centers. Annals of Surgery. 2011; 254(1):67–72. DOI: 10.1097/SLA.0b013e31821d4bf6 [PubMed: 21532466]

31. Prasad GA, Wu TT, Wigle DA, et al. Endoscopic and Surgical Treatment of Mucosal (T1a) Esophageal Adenocarcinoma in Barrett's Esophagus. Gastroenterology. 2009; 137(3):815–23. [PubMed: 19524578]

32. Steyerberg EW, Neville B, Weeks JC, Earle CC. Referral Patterns, Treatment Choices, and Outcomes in Locoregional Esophageal Cancer: A Population-Based Analysis of Elderly Patients. Journal of Clinical Oncology. 2007; 25(17):2389–96. [PubMed: 17557952]

33. Abate E, DeMeester SR, Zehetner J, et al. Recurrence after Esophagectomy for Adenocarcinoma: Defining Optimal Follow-Up Intervals and Testing. Journal of the American College of Surgeons. 2010; 210(4):428–35. [PubMed: 20347734]

34. Wani S, Das A, Rastogi A, et al. Endoscopic ultrasonography in esophageal cancer leads to improved survival rates: Results from a population-based study. Cancer. 2015; 121(2):194–201. [PubMed: 25236485]

35. Young PE, Gentry AB, Acosta RD, Greenwald BD, Riddle M. Endoscopic Ultrasound Does Not Accurately Stage Early Adenocarcinoma or High-Grade Dysplasia of the Esophagus. Clinical Gastroenterology and Hepatology. 2010; 8(12):1037–41. [PubMed: 20831900]

36. Ra J, Paulson EC, Kucharczuk J, et al. Postoperative Mortality After Esophagectomy for Cancer: Development of a Preoperative Risk Prediction Model. Annals of Surgical Oncology. 2008; 15(6):1577–84. [PubMed: 18379852]

37. Derogar M, Orsini N, Sadr-Azodi O, Lagergren P. Influence of major postoperative complications on health-related quality of life among long-term survivors of esophageal cancer surgery. Journal of Clinical Oncology. 2012; 30(14):1615–9. [PubMed: 22473157]

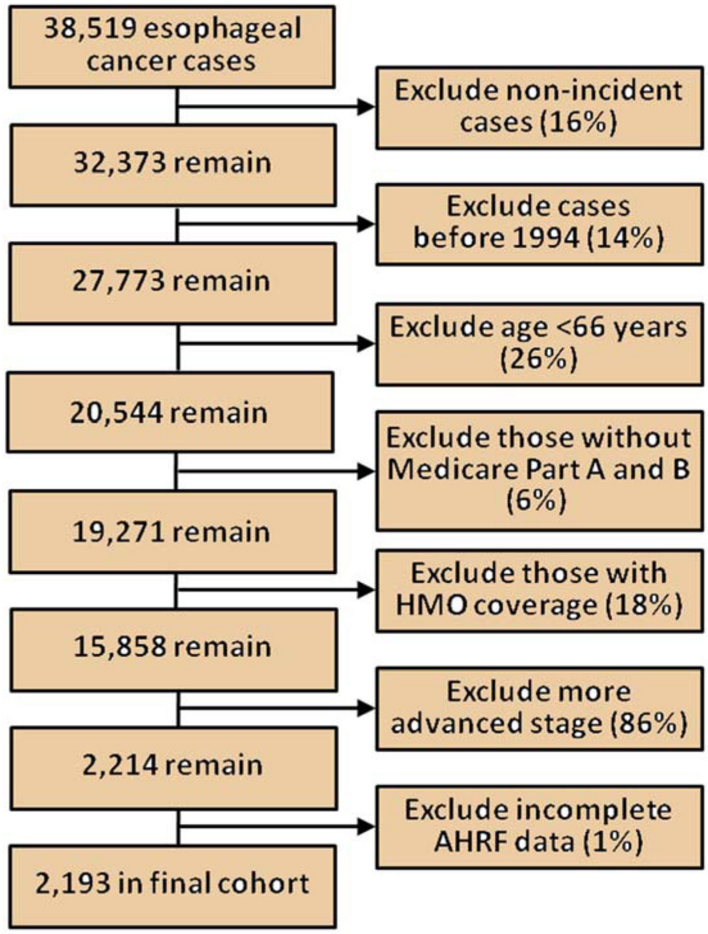

Figure 1.

Stepwise patient selection flowsheet. Percentage in parentheses indicates the proportion of patients excluded at each step. HMO, Health Maintenance Organization; AHRF; Area Health Resources Files

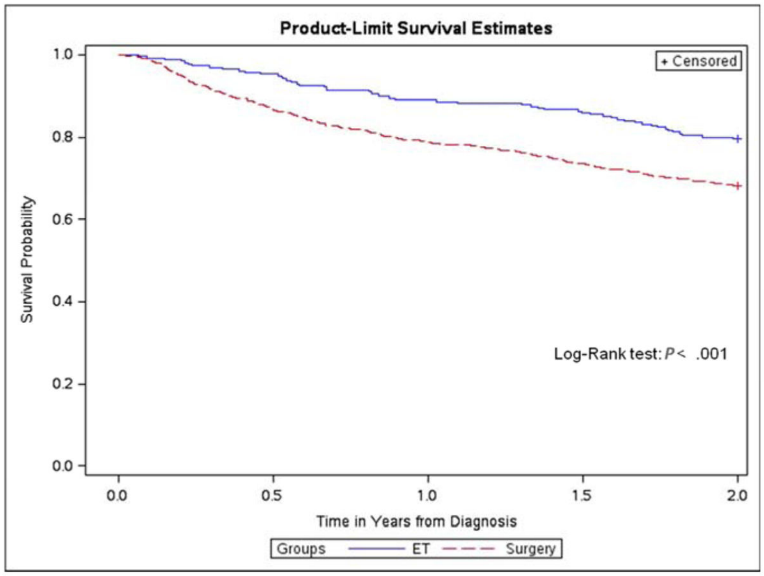

Figure 2.

Kaplan-Meier overall survival curves for patients undergoing endoscopic treatment versus surgical resection for early esophageal cancer. ET, Endoscopic Treatment.

Table 1

Demographic characteristics in cohort by treatment approach

	Treatment Approach				
	No surgery or ET (n=1045)	Surgery (n=893)	ET (n=255)	P value (Surgery vs. ET)	P value (all 3 groups)
Mean Age (SD)	78.6 (6.9)	74.3 (5.4)	77.5 (6.4)	<0.0001	<0.0001
Female	367 (35.1)	202 (22.6)	58 (22.8)	0.97	<0.0001
Race					
White	856 (81.9)	822 (92.1)	238 (93.3)	0.50	<0.0001
Black/Other	189 (18.1)	71 (8.0)	17 (6.7)		
Histologic Subtype					
Adenocarcinoma	502 (48.0)	632 (70.8)	177 (69.4)	0.67	<0.0001
SCC	543 (52.0)	261 (29.2)	78 (30.6)		
T stage					
Tis	136 (13.0)	88 (9.9)	60 (23.5)	<0.0001	<0.0001
T1a	909 (87.0)	805 (90.2)	195 (76.5)		
Charlson Score					
0	249 (23.8)	238 (26.7)	47 (18.4)	0.006	0.002
1	687 (65.7)	599 (67.1)	182 (71.4)		
≥2	109 (10.4)	56 (6.3)	26 (10.2)		
Radiation	610 (58.4)	165 (18.5)	35 (13.7)	0.08	<0.0001
Gastroenterologist Density (per 1,000 residents)					
Q1: 0–<0.026	239 (22.9)	221 (24.8)	61 (23.9)	0.87	0.76
Q2: 0.026–<0.042	278 (26.6)	227 (25.4)	63 (24.7)		
Q3: 0.042–<0.066	260 (24.9)	240 (26.9)	66 (25.9)		
Q4: 0.066–0.183	268 (25.7)	205 (23.0)	65 (25.5)		
Primary Care Provider Density (per 1,000 residents)					
Q1: 0–<0.183	261 (25.0)	225 (25.2)	62 (23.3)	0.89	0.99
Q2: 0.183–<0.263	220 (21.1)	197 (22.1)	54 (21.2)		
Q3: 0.263–<0.352	309 (29.6)	261 (29.2)	73 (28.6)		
Q4: 0.356–0.851	255 (24.4)	210 (23.5)	66 (25.9)		

	Treatment Approach				
	No surgery or ET (n=1045)	Surgery (n=893)	ET (n=255)	P value (Surgery vs. ET)	P value (all 3 groups)
Education[†]					
Q1: 0–<13.6	211 (20.2)	176 (19.7)	47 (18.4)	0.19	0.17
Q2: 13.6–<18.5	265 (25.4)	213 (23.9)	69 (27.1)		
Q3: 18.5–<23.2	304 (29.1)	307 (34.4)	72 (28.2)		
Q4: 23.2–45.7	265 (25.4)	197 (22.1)	67 (26.3)		
Income[‡]					
Q1: $0–<$46,452	272 (26.0)	197 (22.1)	55 (21.6)	0.63	0.27
Q2: $46,452–<$53,438	263 (25.2)	241 (27.0)	66 (25.9)		
Q3: $53,438–<$64,611	238 (22.8)	231 (25.9)	60 (23.5)		
Q4: ≥$64,611	272 (26.0)	224 (25.1)	74 (29.0)		
SEER Registry Region					
Northeast	237 (22.7)	203 (22.7)	71 (27.8)	0.34	0.22
Midwest	132 (12.6)	137 (15.3)	33 (12.9)		
South	227 (21.7)	170 (19.0)	44 (17.3)		
West	449 (43.0)	383 (42.9)	107 (42.0)		

ET, Endoscopic Treatment

SD, Standard Deviation

SCC, Squamous cell carcinoma

Q, Quartile

Data are presented as frequency (%) unless otherwise specified

[†] Mean % residents in county with college education

[‡] Mean county-level median income

Table 2

Cox model stratified by histology identifying predictors of overall mortality (2-year survival)

Variable	Univariable		Multivariable	
	HR (95%CI)	P value	HR (95%CI)	P value
ET vs. surgery	0.57 (0.43, 0.77)	0.0002	0.51 (0.36, 0.73)	0.0002
Age at diagnosis	1.04 (1.02, 1.06)	<0.0001	1.07 (1.04, 1.09)	<0.0001
Female gender vs. male	0.80 (0.61, 1.04)	0.10	0.75 (0.55, 1.03)	0.07
Black/Other race vs. white	1.18 (0.81, 1.71)	0.40	1.10 (0.71, 1.71)	0.67
Tis vs. T1a	0.55 (0.38, 0.81)	0.002	0.65 (0.44, 0.98)	0.04
Charlson Score				
0	Reference		Reference	
1	1.08 (0.84, 1.40)	0.55	1.10 (0.81, 1.49)	0.54
≥2	1.52 (1.01, 2.29)	<0.05	1.54 (0.93, 2.53)	0.09
Receipt of radiation	1.74 (1.36, 2.21)	<0.0001	1.52 (1.14, 2.03)	0.004
SEER Registry Region				
Northeast	Reference		Reference	
Midwest	1.12 (0.78, 1.62)	0.54	1.20 (0.68, 2.10)	0.53
South	1.56 (1.13, 2.15)	0.007	1.59 (0.97, 2.60)	0.07
West	1.15 (0.87, 1.54)	0.33	1.40 (0.85, 2.31)	0.19
Education[†]				
Q1: 0–<13.6	1.70 (1.21, 2.40)	0.002	0.91 (0.49, 1.71)	0.77
Q2: 13.6–<18.5	1.41 (1.01, 1.97)	<0.05	1.19 (0.71, 1.99)	0.52
Q3: 18.5–<23.2	1.60 (1.17, 2.18)	0.003	1.42 (0.93, 2.16)	0.10
Q4: 23.2–45.7	Reference		Reference	
Income[‡]				
Q1: $0–<$46,452	1.76 (1.29, 2.42)	0.0004	2.01 (1.09, 3.72)	0.03
Q2: $46,452–<$53,438	1.47 (1.08, 2.01)	0.02	1.07 (0.63, 1.80)	0.81
Q3: $53,438–<$63,611	1.26 (0.91, 1.74)	0.16	0.99 (0.61, 1.62)	0.97
Q4: ≥$64,611	Reference		Reference	
Gastroenterologist density (per 1,000 residents)				
Q1: 0–<0.026	1.23 (0.91, 1.67)	0.18	0.94 (0.58, 1.55)	0.82
Q2: 0.026–<0.042	0.95 (0.69, 1.30)	0.73	0.91 (0.57, 1.44)	0.68
Q3: 0.042–<0.066	1.17 (0.87, 1.58)	0.30	1.11 (0.74, 1.66)	0.61
Q4: 0.066–0.183	Reference		Reference	
Primary Care Provider Density (per 1,000 residents)				
Q1: 0–<0.183	1.11 (0.81, 1.50)	0.52	0.95 (0.47, 1.94)	0.89
Q2: 0.183–<0.263	1.16 (0.85, 1.58)	0.36	1.29 (0.71, 2.33)	0.41
Q3: 0.263–<0.352	1.03 (0.76, 1.39)	0.86	1.63 (1.01, 2.63)	0.04
Q4: 0.352–0.851	Reference		Reference	

Variable	Univariable		Multivariable	
	HR (95%CI)	P value	HR (95%CI)	P value
Diagnosis 2002–2009 vs. 1994–2001	0.63 (0.50, 0.78)	<0.0001	0.62 (0.47, 0.81)	<0.001

ET, Endoscopic Treatment

HR, Hazard Ratio

CI, Confidence Interval

Q, Quartile

†Mean % residents in zip code with college education

‡Mean zip code median income