Published in final edited form as:

Cancer. 2009 November 1; 115(21): 4924–4933. doi:10.1002/cncr.24536.

Esophagectomy Compared to Chemoradiation for Early Stage Esophageal Cancer in the Elderly

Julian A. Abrams^{1,2}, Donna L. Buono³, Joshua Strauss⁴, Russell B. McBride³, Dawn L. Hershman^{1,2,3}, and Alfred I. Neugut^{1,2,3}

¹Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY

²Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY

³Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY

⁴Albert Einstein College of Medicine, New York, NY

Abstract

Background—Esophagectomy has been the traditional treatment of choice for early stage esophageal cancer. However, esophagectomy is associated with high mortality and morbidity in the elderly, and these patients often receive chemoradiation instead. We compared outcomes of esophagectomy versus chemoradiation in a population-based sample of elderly patients with early stage esophageal cancer.

Methods—We used the Surveillance, Epidemiology, and End Results-Medicare database to identify patients ≥ 65 years diagnosed with stage 1 or 2 esophageal cancer from 1991–2002. We assessed associations of treatment with esophagectomy or chemoradiation with demographic and clinical variables. We performed survival analyses to compare outcomes with treatment modality, adjusted for potential confounders.

Results—We identified 730 patients with stage 1 or 2 esophageal cancer who underwent esophagectomy ($n=341$; 46.7%) or chemoradiation ($n=389$, 53.3%). Older age, squamous cell histology, and lower socioeconomic status were associated with increased odds of receipt of chemoradiation. In multivariable analyses, chemoradiation was associated with worse disease-specific (HR 2.08, 95%CI 1.64–2.64) and overall survival (HR 1.92, 95%CI 1.58–2.34). Receipt of chemoradiation was associated with worse survival for adenocarcinoma (HR 3.01, 95%CI 2.24–4.04), but there was no significant difference for squamous cell (HR 1.33, 95%CI 0.98–1.80).

Conclusion—Compared to chemoradiation, esophagectomy may be associated with improved survival for early stage esophageal cancer in the elderly. The results suggest that there may also be a subset of squamous cell patients for whom chemoradiation is adequate therapy. A randomized trial would be useful to determine optimal treatment for elderly patients with early stage esophageal cancer.

Keywords

esophageal cancer; esophagectomy; chemotherapy; radiotherapy; SEER; Medicare; epidemiology

Corresponding author: Julian A. Abrams, MD, MS, Black Building 10-508, 630 W. 168th Street, New York, NY 10032, Phone: (212) 342-0476, Fax: (212) 305-6443, e-mail: ja660@columbia.edu.

The authors have no financial disclosures to report.

INTRODUCTION

Esophageal cancer continues to be associated with a poor prognosis, with a 5-year survival rate of 16%.¹ Traditionally, esophagectomy has been the primary curative treatment for esophageal cancer. Unfortunately, esophagectomy is associated with a 5% surgical mortality rate even at high volume centers, and a 10% mortality rate overall in the United States.^{2, 3} The average age at diagnosis of esophageal cancer is 69 years; older age is a risk factor for worse surgical outcomes with esophagectomy.^{3, 4}

Clinical trials from the 1990s demonstrated that combined chemoradiation (CRT) was superior to radiation therapy alone.^{5, 6} More recent studies have evaluated the utility of neoadjuvant CRT followed by esophagectomy, although the results for this have been mixed.^{7–10} Two randomized clinical trials suggested that, in squamous cell carcinoma of the esophagus, survival with chemoradiation (CRT) alone may be equivalent to CRT followed by surgery.^{11, 12} The current National Comprehensive Cancer Network (NCCN) guidelines recommend esophagectomy alone for stage 1 disease (or endoscopic resection for intramucosal carcinoma), and optional neoadjuvant therapy for stage 2 disease.¹³ However, given the high operative mortality associated with esophagectomy, many elderly patients are referred for nonoperative treatment of esophageal cancer, i.e., definitive CRT alone.¹⁴ There are no published randomized trials to date that compare CRT versus surgery alone for the treatment of esophageal cancer.

In most of the clinical trials for esophageal cancer from the 1990s, the majority of patients had squamous cell cancer. In Western countries, the incidence of esophageal adenocarcinoma is rising rapidly and is now the predominant cell type.¹⁵ There is very little published on nonoperative management strategies specifically for esophageal adenocarcinoma. Given the changing epidemiology of esophageal cancer, the high operative mortality of esophagectomy, and recent data suggesting the efficacy of CRT alone for squamous cell cancer, we decided to perform a population-based study that compared esophagectomy to CRT for patients with early stage esophageal cancer.

METHODS

Data Source

We analyzed patient data from the linked Surveillance, Epidemiology, and End Results (SEER) – Medicare database.¹⁶ The SEER database contains records of patients diagnosed with cancer in regions representing approximately 26% of the US population. SEER provides information on tumor histology, location, stage of disease, treatment, and survival, along with selected census tract-level demographic information. The Medicare database includes Medicare A and B eligibility status, dates of enrollment onto health maintenance organization, and billed claims, including inpatient and outpatient services, procedures, and diagnoses.

Sample selection

We identified all individuals in the linked SEER-Medicare database diagnosed with primary esophageal cancer (International Classification of Diseases – 9th Revision [ICD-9] codes: 150.0–150.9) from January 1, 1991 to December 31, 2002 (n=15,980), who had esophageal cancer as first primary malignancy and age ≥65 years (n=10,389). We excluded 1,127 patients for the following reasons: original reason for Medicare entitlement was not age ≥65; date of death in SEER and Medicare differed by >3 months; reporting source of death was autopsy or death certificate. We excluded an additional 3,418 patients who were enrolled in a health maintenance organization (HMO) at any point from 12 months before to 6 months after date of diagnosis and/or were not covered by Medicare Parts A and B at any

point during that time period. An additional 3,995 patients were excluded with in situ disease, American Joint Committee on Cancer stage 3 or 4 disease, or if T or N staging was unknown. There were 1,559 patients with histologically confirmed esophageal cancer and stage 1 (T1N0) or 2 (T2N0, T3N0, T1N1, T2N1). Of these, 829 patients were excluded for the following reasons: unknown radiation status; first treatment more than 4 months after the date of diagnosis; receipt of chemotherapy and/or radiation prior to surgery; receipt of chemotherapy and/or radiation within 4 months of surgery; receipt of chemotherapy or radiation alone, but not both.

The SEER database includes age, race/ethnicity, sex, marital status, and area of residence. Age at diagnosis was broken down into pentads (5-year discrete numeric intervals) starting at 65 years. Because the sample included few patients who were neither black nor white, we designate race as black, white, or other. For similar reasons, we recoded the SEER marital status variable into married, not married, and unknown.

The subjects included in the analyses were categorized by treatment received (esophagectomy or CRT), age group at diagnosis, year of diagnosis, race/ethnicity, gender, marital status, tumor stage (1 or 2), tumor grade (well/moderately differentiated or poorly differentiated), comorbidity score, residence (rural vs. urban area), and socioeconomic status quintile.

Esophagectomy group

We identified all patients who underwent an esophagectomy within 4 months of the date of diagnosis, using Current Procedural Terminology (CPT) codes (43100, 43101, 43107, 43108, 43112, 43113, 43116-8, 43121-4) and ICD-9 surgery codes (424, 4240-2, 4399). Any patient who received chemotherapy and/or radiation therapy at any time prior to the date of surgery or within 4 months after the date of surgery was excluded from analysis. Receipt of chemotherapy or radiation more than 4 months after surgery was considered likely to be treatment for recurrent disease, and these patients remained in the esophagectomy only group.

Chemoradiation (CRT) group

We identified all patients who received both chemotherapy and radiation therapy started within 4 months of the date of diagnosis. Receipt of chemotherapy was defined by Healthcare Common Procedure Coding Systems (HCPCS) codes J9000-J9999. Receipt of radiation therapy was defined by the following codes: ICD-9 V580, V671, 9220-9; CPT 77331-6, 77370, 77399, 77401-4, 77406-9, 77411-4, 77416-20, 77422, 77423, 77425, 77427, 77430-2, 77435, 77470, 77499, 77750, 77761-3, 77776-8, 77781-4, 77789, 77790, 77799. Any patient who had an esophagectomy was not included in this group. Any patient who had chemotherapy without radiation or radiation without chemotherapy was excluded from analysis.

The validity of SEER-Medicare claims data for chemotherapy use has been previously described.^{17, 18} Medicare claims are generated for diagnostic procedures, diagnoses, and treatments for which hospitals and physicians bill, including, for cancer patients, intravenous and injectable chemotherapy.

Socioeconomic status

We generated an aggregate SES score from a hierarchy of income data from the 2000 census, following the method described by Du et al.¹⁹ Patients were grouped into quintiles, based on a formula incorporating data related to income, poverty, and education. Patients for whom all these values were missing were assigned to the lowest SES category.

Comorbid disease

We computed a comorbidity score for each patient using the variables included in the Klabunde adaptation of the Charlson comorbidity index.^{20–22} Medicare inpatient and outpatient claims were searched from 365 days before to 30 days after the diagnosis of esophageal cancer for all ICD-9-Clinical Modification (CM) diagnostic codes corresponding to each of the following comorbid conditions: myocardial infarction; congestive heart failure; peripheral vascular disease; cerebrovascular disease; dementia; chronic pulmonary disease; connective tissue disease; peptic ulcer disease; mild to severe liver disease; diabetes with/without end organ damage; hemiplegia; moderate or severe renal disease; and AIDS. Each condition was weighted, and patients were assigned a score based on the Klabunde-Charlson index.²²

Statistical Analysis

We used chi-square tests to compare patients who underwent esophagectomy or received CRT with respect to clinical and demographic factors. We used logistic regression to estimate odds ratios and 95% confidence intervals for factors associated with treatment with either esophagectomy or CRT. The variables included in this model were: gender; age; year of diagnosis; marital status; race/ethnicity; residence (urban or rural); socioeconomic status; comorbid disease score; tumor stage; and tumor grade. Kaplan-Meier survival curves were generated and compared using the log-rank test. To estimate the association between type of treatment and death from either esophageal cancer or from any cause, while controlling for the other covariates, we used conventional Cox proportional hazards models. Given the relatively small sample size and potential for significant selection bias, we repeated the regression analyses using propensity scoring in order to better estimate the treatment group effect.²³ All analyses were conducted using SAS Version 9.13 (SAS Institute, Cary, NC).

This study was approved by the Columbia University Institutional Review Board.

RESULTS

We identified a total of 730 patients with stage 1 or 2 esophageal cancer who were treated with either chemoradiation (CRT) or esophagectomy alone between 1991 and 2002 (**Table 1**). Slightly more than half of these patients received CRT (53.3%), and 46.7% underwent esophagectomy. There were 354 cases (48.5%) with adenocarcinomas and 303 (41.5%) with squamous cell carcinomas, with the remainder classified as other or unknown (10.0%, n=73). There were 409 patients (56.0%) with stage 1 disease and 321 (44.0%) with stage 2 disease.

Factors associated with receipt of CRT (versus esophagectomy) are shown in Table 2. Patients with adenocarcinoma were significantly less likely to receive CRT (OR 10.24, 95% CI 0.16–0.35), as were patients with stage 2 disease (OR 0.67, 95% CI 0.48–0.94).

Overall survival in the esophagectomy group was significantly better than in the group that received CRT (Figure 1). These differences were more pronounced for adenocarcinoma than for squamous cell cancer. Three-year and five-year overall and disease-specific survival rates are shown in Table 3. In multivariable Cox analyses, receipt of CRT was associated with significantly worse disease-specific (HR 2.08, 95% CI 1.64–2.64) and overall survival (HR 1.92, 95% CI 1.58–2.34) (Table 4). Other factors associated with worse overall survival included stage 2 disease, poorly differentiated tumors, increased comorbidities, and older age. Black race was associated with improved overall survival. Among patients who underwent esophagectomy, 24 (7.7%) died within 30 days of the date of surgery.

We hypothesized that there was a potentially strong selection bias with regard to receipt of CRT or esophagectomy. We therefore repeated the analyses using propensity scoring in order to better estimate the treatment group effect. Receipt of CRT remained strongly associated with worse disease-specific (HR 2.21, 95%CI 1.74–2.81) as well as overall survival (HR 2.05, 95%CI 1.68–2.49).

In multivariable analyses stratified by cell type, CRT in adenocarcinoma patients was associated with significantly worse disease-specific and overall survival (Table 5). In patients with squamous cell carcinoma, however, there was no significant difference in survival between CRT and esophagectomy. Separate stratified analyses were also performed by tumor stage. Receipt of CRT in stage 1 patients was associated with higher risks of esophageal cancer-specific mortality than in patients with stage 2 disease (Stage 1: HR 3.50, 95%CI 2.40–5.11; Stage 2: HR 1.32, 95%CI 0.95–1.83).

In order to better assess the treatment group effect without the impact of early death, multivariable analyses were also performed after excluding patients who died within four months. Receipt of CRT was again associated with worse disease-specific (HR 2.61, 95%CI 2.01–3.39) and overall survival (HR 2.46, 95%CI 1.98–3.05).

DISCUSSION

In our population-based study of elderly patients with early stage esophageal cancer, esophagectomy was associated with improved disease-free and overall survival as compared to combined chemoradiation. These findings were most apparent for patients with adenocarcinoma and in those with stage 1 disease.

The decision whether to perform esophagectomy on an elderly patient with esophageal cancer is often difficult to make and encompasses many immeasurable factors. Several steps were taken to exclude patients who did not undergo esophagectomy due to very poor baseline health status. The nonoperative treatment group received both chemo- and radiation therapy (not just one or the other), we adjusted for comorbidities in the final multivariable models, and the analyses were repeated using propensity scoring, an analytic method used to minimize the effects of selection bias in a non-randomized study.²³ Additionally, the analyses were repeated, excluding patients who died within four months of treatment (esophagectomy or CRT), in order to exclude the sickest patients who may have been unevenly distributed between the two treatment groups. The results from all of these analyses demonstrated a consistent two to three-fold improved disease-free and overall survival in those patients who underwent esophagectomy. However, these statistical methods can only partially overcome the effects of the powerful selection bias inherent to the study question that we attempted to address.

Interestingly, stage 2 patients were more likely than stage 1 to receive esophagectomy. The reasons for this finding are not clearly intuitive, as one would anticipate that ability to tolerate esophagectomy would be inversely correlated with tumor stage. We suspect that a greater proportion of patients with stage 2 disease who were unfit to tolerate surgery or CRT may have been excluded from the analyses, resulting in a healthier group more likely to undergo esophagectomy. Older age was associated with increased odds of receipt of CRT; older age is a known risk factor for surgical morbidity and mortality after esophagectomy.³

We found squamous cell histology to be strongly associated with receipt of chemoradiation. Cervical and upper esophageal tumors are almost exclusively of squamous cell histology, and tumors of this region can be technically more difficult to resect due to proximity to the major airways and potential for local invasion. There are published retrospective series of patients with localized squamous cell cancer that report comparable outcomes between CRT

and esophagectomy.^{24–26} As such, some medical oncologists may have been more likely to refer “borderline” surgical candidates with squamous cell cancer for chemoradiation instead of surgery.

Our results support the notion that response to CRT in esophageal cancer varies greatly by cell type. We found a large survival advantage for esophagectomy in patients with adenocarcinoma, whereas there was no significant difference in survival between CRT and esophagectomy in squamous cell patients. It is possible that there is a small benefit to esophagectomy over CRT in squamous cell cancer, and our study may have been simply underpowered to detect this survival difference.

There are randomized clinical trials that suggest that CRT may have comparable outcomes to esophagectomy in squamous cell cancer.^{11, 12} In a study locally advanced esophageal squamous cell cancer, there was no significant difference in overall survival between CRT alone and CRT followed by esophagectomy.¹¹ However, the survival curves diverged at 2 years in favor of CRT plus esophagectomy. Our survival curves for patients with squamous cell cancer followed a similar pattern, possibly indicative of disease recurrence 2 years after treatment with chemoradiation.

In stratified analyses, we found a larger survival benefit for esophagectomy in stage 1 disease than in stage 2 disease. A recent retrospective multicenter study reported low incidences of systemic disease after esophagectomy alone for early stage disease.²⁷ However, according to NCCN guidelines, neoadjuvant treatment with chemotherapy or chemoradiation is acceptable for stage 2 disease.¹³ As neoadjuvant therapy is not recommended for stage 1 disease, the observed survival benefit for esophagectomy in this group may more closely reflect the true effect of this treatment.

Interestingly, blacks had better all cause and esophageal cancer-specific survival as compared to whites. In a SEER analysis by Greenstein et al.²⁸, black race was associated with a nonsignificant increased risk of death from any cause; however, more than 50% of the patients did not receive either surgery or radiation. Blacks are less likely to receive radiation or chemotherapy or undergo surgery for esophageal cancer¹⁴, and the disparate findings may be explained in part by the fact that, in the current study, blacks and whites all received treatment (esophagectomy or CRT).

The current study has several strengths. We compared two distinct treatment options for early stage esophageal cancer, esophagectomy and CRT, as opposed to a single treatment compared to partial or no treatment. By performing stratified analyses, we were able to identify particular subgroups in whom esophagectomy was associated with better outcomes (stage 1 disease, adenocarcinoma) and others in whom CRT may be a reasonable alternative (squamous cell cancer). Many immeasurable factors go into a decision whether or not to perform esophagectomy on a patient with esophageal cancer, thus introducing potential selection bias. Propensity scoring serves to minimize the effects of selection bias in a nonrandomized study, and these analyses also demonstrated a consistent benefit for esophagectomy.

There are certain limitations to our analyses. Tumor staging is most accurate in patients who undergo esophagectomy. Clinical staging in the CRT group was presumably based on endoscopic ultrasound, computed tomography, or other tests, and it is not clear in what direction the results would have been biased. The TNM tumor stage reported in SEER is derived from a computer algorithm that combines elements of pathologic and clinical data to derive a “best stage”, which limits our ability to perform analyses to assess the accuracy of clinical staging in this dataset.

Despite our best efforts to minimize its effects, selection bias may still have a significant impact on our findings. While the present study reports death from esophageal cancer or from any cause as the primary outcomes, we did not evaluate other important outcomes, such as the need for eventual palliative interventions. The results of one randomized trial showed that, despite a lack of benefit with regard to overall survival, esophagectomy (as compared to CRT) was associated with significantly fewer palliative stenting procedures for recurrent disease.¹²

Despite the high surgical mortality associated with esophagectomy for esophageal cancer, the results of our analyses suggest that surgery alone may be associated with significantly improved overall and disease-specific survival compared to CRT for the treatment of early stage esophageal cancer in the elderly. The findings were most evident for patients with esophageal adenocarcinoma. There may be a subgroup of esophageal squamous cell cancer patients in whom CRT is an acceptable alternative to esophagectomy. Given the potentially strong selection bias inherent to the present study design, a randomized clinical trial including adequate numbers of both cell types is needed to confirm the optimal treatment for early stage esophageal cancer in the elderly.

Acknowledgments

We would like to thank Dr. Nasser Altorki for his critical input in the data interpretation.

Supported in part by a Young Clinical Scientist Award to Dr. Abrams from the Flight Attendant Medical Research Institute, grants from the American Cancer Society to Dr. Hershman (ACS 114106 RSGT) and Dr. Neugut (RSGT-01-024-04-CPHPS). Mr. McBride was supported by an R25 fellowship from the NCI (CA094061) and a T32 fellowship (UL1 RR024156) from the National Center for Research Resources.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. *CA Cancer J Clin*. 2008; 58(2):71–96. [PubMed: 18287387]
2. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. *N Engl J Med*. 2003; 349(22):2117–2127. [PubMed: 14645640]
3. Steyerberg EW, Neville BA, Koppert LB, Lemmens VE, Tilanus HW, Coebergh JW, et al. Surgical mortality in patients with esophageal cancer: development and validation of a simple risk score. *J Clin Oncol*. 2006; 24(26):4277–4284. [PubMed: 16963730]
4. Ries, LAG.; Melbert, D.; Krapcho, M.; Stinchcomb, DG.; Howlader, N.; Horner, MJ., et al. SEER Cancer Statistics Review, 1975–2005. Bethesda, MD: National Cancer Institute; [Accessed on 9 Sept 2008]. Available from http://seer.cancer.gov/csr/1975_2005/:
5. Herskovic A, Martz K, al-Sarraf M, Leichman L, Brindle J, Vaitkevicius V, et al. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. *N Engl J Med*. 1992; 326(24):1593–1598. [PubMed: 1584260]
6. Cooper JS, Guo MD, Herskovic A, Macdonald JS, Martenson JA Jr, Al-Sarraf M, et al. Radiation Therapy Oncology Group. Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RTOG 85-01). *Jama*. 1999; 281(17):1623–1627. [PubMed: 10235156]
7. Tepper J, Krasna MJ, Niedzwiecki D, Hollis D, Reed CE, Goldberg R, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. *J Clin Oncol*. 2008; 26(7):1086–1092. [PubMed: 18309943]
8. Walsh TN, Noonan N, Hollywood D, Kelly A, Keeling N, Hennessy TP. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. *N Engl J Med*. 1996; 335(7):462–467. [PubMed: 8672151]

9. Bosset JF, Gignoux M, Triboulet JP, Tiet E, Mantion G, Elias D, et al. Chemoradiotherapy followed by surgery compared with surgery alone in squamous-cell cancer of the esophagus. *N Engl J Med*. 1997; 337(3):161–167. [PubMed: 9219702]
10. Burmeister BH, Smithers BM, Gebisi V, Fitzgerald L, Simes RJ, Devitt P, et al. Surgery alone versus chemoradiotherapy followed by surgery for resectable cancer of the oesophagus: a randomised controlled phase III trial. *Lancet Oncol*. 2005; 6(9):659–668. [PubMed: 16129366]
11. Stahl M, Stuschke M, Lehmann N, Meyer HJ, Walz MK, Seeber S, et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. *J Clin Oncol*. 2005; 23(10):2310–2317. [PubMed: 15800321]
12. Bedenne L, Michel P, Bouche O, Milan C, Mariette C, Conroy T, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. *J Clin Oncol*. 2007; 25(10):1160–1168. [PubMed: 17401004]
13. Ajani, JA.; Bekaii-Saab, T.; Osarogiagbon, RU.; Yang, G. Practice guidelines in oncology - Esophageal cancer. Fort Washington, PA: National Comprehensive Cancer Network; [Accessed on 10 Sept 2008]. Available from http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf
14. 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. *J Clin Oncol*. 2007; 25(17):2389–2396. [PubMed: 17557952]
15. Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. *J Natl Cancer Inst*. 2008; 100(16):1184–1187. [PubMed: 18695138]
16. Potosky AL, Riley GF, Lubitz JD, Mentnech RM, Kessler LG. Potential for cancer related health services research using a linked Medicare-tumor registry database. *Med Care*. 1993; 31(8):732–748. [PubMed: 8336512]
17. Warren JL, Harlan LC, Fahey A, Virnig BA, Freeman JL, Klabunde CN, et al. Utility of the SEER-Medicare data to identify chemotherapy use. *Med Care*. 2002; 40(8 Suppl):IV-55–IV-61.
18. Lamont EB, Lauderdale DS, Schilsky RL, Christakis NA. Construct validity of medicare chemotherapy claims: the case of 5FU. *Med Care*. 2002; 40(3):201–211. [PubMed: 11880793]
19. Du XL, Fang S, Vernon SW, El-Serag H, Shih YT, Davila J, et al. Racial disparities and socioeconomic status in association with survival in a large population-based cohort of elderly patients with colon cancer. *Cancer*. 2007; 110(3):660–669. [PubMed: 17582625]
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987; 40(5):373–383. [PubMed: 3558716]
21. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992; 45(6):613–619. [PubMed: 1607900]
22. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol*. 2000; 53(12):1258–1267. [PubMed: 11146273]
23. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998; 17(19):2265–2281. [PubMed: 9802183]
24. Chan A, Wong A. Is combined chemotherapy and radiation therapy equally effective as surgical resection in localized esophageal carcinoma? *Int J Radiat Oncol Biol Phys*. 1999; 45(2):265–270. [PubMed: 10487544]
25. Delcambre C, Jacob JH, Pottier D, Gignoux M, Ollivier JM, Vie B, et al. Localized squamous-cell cancer of the esophagus: retrospective analysis of three treatment schedules. *Radiother Oncol*. 2001; 59(2):195–201. [PubMed: 11325449]
26. Hironaka S, Ohtsu A, Boku N, Muto M, Nagashima F, Saito H, et al. Nonrandomized comparison between definitive chemoradiotherapy and radical surgery in patients with T(2–3)N(any) M(0) squamous cell carcinoma of the esophagus. *Int J Radiat Oncol Biol Phys*. 2003; 57(2):425–433. [PubMed: 12957254]
27. Peyre CG, Hagen JA, DeMeester SR, Van Lanschot JJ, Holscher A, Law S, et al. Predicting systemic disease in patients with esophageal cancer after esophagectomy: a multinational study on

the significance of the number of involved lymph nodes. *Ann Surg.* 2008; 248(6):979–985. [PubMed: 19092342]

28. Greenstein AJ, Litle VR, Swanson SJ, Divino CM, Packer S, McGinn TG, et al. Racial disparities in esophageal cancer treatment and outcomes. *Ann Surg Oncol.* 2008; 15(3):881–888. [PubMed: 17987341]

Figure 1. Kaplan-Meier curves for overall survival comparing esophagectomy with chemoradiation in elderly patients with stage 1 and 2 esophageal cancer. A) All cell types; B) Adenocarcinoma only; C) Squamous cell cancer only

Figure 2.

Figure 3.

Table 1

Characteristics of patients with early stage esophageal cancer who underwent esophagectomy or received chemoradiation (CRT), SEER-Medicare 1991–2002.

	Total	Esophagectomy	CRT	p-value
Patients	730	341 (46.7%)	389 (53.3%)	
Male gender	518 (71.0%)	257 (75.4%)	261 (67.1%)	0.01
Age				<0.001
65–69	170 (23.3%)	98 (28.7%)	72 (18.5%)	
70–74	212 (29.0%)	108 (31.7%)	104 (26.8%)	
75–79	202 (27.7%)	84 (24.6%)	118 (30.3%)	
≥80	146 (20.0%)	51 (15.0%)	95 (24.4%)	
Race				0.002
White	636 (87.1%)	306 (89.7%)	330 (84.8%)	
Black	41 (7.4%)	13 (3.8%)	41 (10.6%)	
Other/Unknown	40 (5.5%)	22 (6.5%)	18 (4.6%)	
Year of diagnosis				<0.001
1991–1993	112 (15.3%)	66 (19.4%)	46 (11.8%)	
1994–1996	154 (21.1%)	87 (25.5%)	67 (17.2%)	
1997–1999	145 (19.9%)	74 (21.7%)	71 (18.3%)	
2000–2002	319 (43.7%)	114 (33.4%)	205 (52.7%)	
Histology				<0.001
Adenocarcinoma	354 (48.5%)	213 (62.5%)	141 (36.3%)	
Squamous cell	303 (41.5%)	94 (27.5%)	209 (53.7%)	
Other/Unknown	73 (10.0%)	34 (10.0%)	39 (10.0%)	
Tumor stage				0.04
1	409 (56.0%)	177 (51.9%)	232 (59.6%)	
2	321 (44.0%)	164 (48.1%)	157 (40.4%)	
Tumor grade				0.015
Well/moderately differentiated	318 (43.6%)	159 (46.6%)	159 (40.9%)	
Poorly differentiated	289 (39.6%)	139 (40.8%)	150 (38.5%)	
Unknown	123 (16.8%)	43 (12.6%)	80 (20.6%)	
No. of comorbidities				0.34
0	300 (41.2%)	148 (43.5%)	152 (39.1%)	
1	232 (31.8%)	108 (31.8%)	124 (31.9%)	
>1	197 (27.0%)	84 (24.7%)	113 (29.0%)	
Urban/Suburban residence	669 (91.6%)	307 (90.0%)	362 (93.1%)	0.14
Married	469 (65.8%)	242 (72.9%)	227 (59.6%)	<0.001
SES quintile				0.11
1 st (lowest)	95 (13.1%)	33 (9.9%)	62 (16.0%)	
2 nd	124 (17.2%)	55 (16.5%)	69 (17.8%)	
3 rd	166 (23.0%)	76 (22.8%)	90 (23.2%)	
4 th	158 (21.9%)	80 (23.9%)	78 (20.1%)	

	Total	Esophagectomy	CRT	p-value
5 th (highest)	179 (24.8%)	90 (26.9%)	89 (22.9%)	

Table 2

Multivariable analysis of factors associated with receipt of chemoradiation (versus surgery alone) for early stage esophageal cancer in the elderly, SEER-Medicare 1991–2002.

	Odds Ratio	95% CI
Patient gender		
Female	1.00	Referent
Male	0.79	0.53–1.19
Age		
65–69	1.00	Referent
70–74	1.48	0.94–2.33
75–79	2.26	1.42–3.60
≥80	2.93	1.75–4.92
Race		
White	1.00	Referent
Black	1.06	0.49–2.32
Other/Unknown	0.41	0.20–0.86
Year of diagnosis		
1991–1993	1.00	Referent
1994–1996	1.06	0.61–1.84
1997–1999	1.28	0.73–2.24
2000–2002	2.71	1.65–4.45
Histology		
Squamous cell	1.00	Referent
Adenocarcinoma	0.24	0.16–0.35
Other/Unknown	0.38	0.21–0.69
Tumor stage		
1	1.00	Referent
2	0.67	0.48–0.94
Tumor grade		
Well/moderately differentiated	1.00	Referent
Poorly differentiated	1.12	0.78–1.61
Unknown	1.87	1.15–3.04
No. of comorbidities		
0	1.00	Referent
1	0.90	0.61–1.34
>1	0.92	0.61–1.40
Residence		
Rural	1.00	Referent
Urban	0.62	0.33–1.15
Marital status		
Unmarried	1.00	Referent
Married	0.67	0.45–0.98
Unknown	0.48	0.16–1.47

	Odds Ratio	95% CI
SES quintile		
1 st (lowest)	1.00	Referent
2 nd	0.71	0.38–1.34
3 rd	0.57	0.31–1.05
4 th	0.47	0.25–0.89
5 th (highest)	0.49	0.27–0.92

Table 3

Three-year and five-year overall and disease-specific survival rates for patients with early stage esophageal cancer, SEER-Medicare 1991–2002.

	3-Year Survival			
	Surgery		Chemoradiation	
	Survival	95% CI	Survival	95% CI
<i>Overall</i>				
All cell types	53.1%	47.6–58.2	23.9%	19.8–28.3
Adenocarcinoma	60.6%	29.5–49.1	21.3%	15.0–28.4
Squamous cell	39.4%	29.5–49.1	25.8%	20.1–31.9
<i>Disease-Specific</i>				
All cell types	63.8%	58.1–68.8	34.1%	28.9–39.3
Adenocarcinoma	72.4%	65.5–78.2	33.0%	24.5–41.8
Squamous cell	48.4%	37.6–58.4	34.7%	27.7–41.7
5-Year Survival				
<i>Overall</i>				
All cell types	44.9%	39.5–50.2	13.9%	10.5–17.9
Adenocarcinoma	50.2%	43.2–56.8	7.5%	3.3–13.9
Squamous cell	35.8%	26.2–45.5	17.1%	12.2–22.7
<i>Disease-Specific</i>				
All cell types	58.3%	52.5–63.7	24.5%	19.4–29.9
Adenocarcinoma	64.9%	57.4–71.4	15.1%	7.2–25.9
Squamous cell	45.8%	35.1–55.9	27.2%	20.6–34.3

Table 4

Multivariable analysis of predictors of death from esophageal cancer and from any cause among patients with early stage esophageal cancer, SEER-Medicare 1991–2002.

	Esophageal cancer		Any cause	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Treatment				
Esophagectomy	1.00	Referent	1.00	Referent
Chemoradiation	2.08	1.64–2.64	1.92	1.58–2.34
Patient gender				
Female	1.00	Referent	1.00	Referent
Male	1.07	0.84–1.38	0.99	0.81–1.22
Age				
65–69	1.00	Referent	1.00	Referent
70–74	0.89	0.67–1.91	0.98	0.77–1.25
75–79	1.01	0.76–1.36	1.19	0.91–1.49
≥80	1.31	0.96–1.79	1.46	1.12–1.90
Race				
White	1.00	Referent	1.00	Referent
Black	0.59	0.38–0.91	0.63	0.44–0.91
Other/Unknown	0.78	0.49–1.26	0.83	0.56–1.22
Year of diagnosis				
1991–1993	1.00	Referent	1.00	Referent
1994–1996	0.85	0.62–1.18	0.94	0.72–1.22
1997–1999	0.70	0.50–0.98	0.80	0.60–1.06
2000–2002	0.76	0.56–1.02	0.84	0.66–1.09
Histology				
Squamous cell	1.00	Referent	1.00	Referent
Adenocarcinoma	0.81	0.63–1.04	0.93	0.76–1.15
Other/Unknown	1.05	0.72–1.53	1.21	0.88–1.65
Tumor stage				
1	1.00	Referent	1.00	Referent
2	1.63	1.32–2.00	1.51	1.27–1.79
Tumor grade				
Well/moderately differentiated	1.00	Referent	1.00	Referent
Poorly differentiated	1.44	1.15–1.80	1.36	1.13–1.63
Unknown	1.03	0.75–1.41	1.16	0.90–1.49
No. of comorbidities				
0	1.00	Referent	1.00	Referent
1	1.42	1.11–1.81	1.51	1.23–1.86
>1	1.57	1.21–2.04	1.86	1.51–2.31
Residence				
Rural	1.00	Referent	1.00	Referent
Urban	1.19	0.82–1.72	1.05	0.77–1.44

	Esophageal cancer		Any cause	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Marital status				
Unmarried	1.00	Referent	1.00	Referent
Married	0.83	0.66–1.05	0.82	0.68–1.00
Unknown	0.42	0.18–0.96	0.47	0.25–0.91
SES quintile				
1 st (lowest)	1.00	Referent	1.00	Referent
2 nd	0.77	0.53–1.13	0.81	0.59–1.10
3 rd	0.76	0.53–1.09	0.73	0.54–0.98
4 th	0.76	0.52–1.11	0.74	0.54–1.01
5 th (highest)	0.84	0.58–1.23	0.75	0.55–1.03

Table 5

Stratified multivariable analyses of risk of death from esophageal cancer and from any cause in patients with early esophageal cancer, SEER-Medicare 1991–2002.

Cause of Death	Cell Type			
	Squamous Cell		Adenocarcinoma	
	HR*	95% CI	HR*	95% CI
<i>Esophageal Cancer</i>				
Esophagectomy	1.00	Referent	1.00	Referent
Chemoradiation	1.34	0.94–1.92	3.84	2.67–5.51
<i>Any cause</i>				
Esophagectomy	1.00	Referent	1.00	Referent
Chemoradiation	1.33	0.98–1.80	3.01	2.24–4.04

* Adjusted for patient gender, age, race, year of diagnosis, stage, tumor grade, comorbidities, residence, marital status, and socioeconomic status.