

Underuse of Esophagectomy as Treatment for Resectable Esophageal Cancer

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Hypothesis: Esophagectomy is underused as treatment for resectable stage I, II, and III esophageal cancers.

Design and Setting: Retrospective cohort study using the Surveillance, Epidemiology, and End Results–Medicare linked database.

Patients: We used the Surveillance, Epidemiology, and End Results database to identify persons 65 years or older who were not enrolled in a health maintenance organization and who were diagnosed as having stage I, II, or III esophageal cancer between January 1, 1997, and December 31, 2002 (N=2386).

Main Outcome Measures: The rate of surgical intervention was compared across varying patient characteristics, including age, race, comorbidity score, sex, tumor stage, and socioeconomic region. Survival was compared between patients who received surgery and those who did not using Kaplan-Meier curves, the log-rank test, and Cox proportional hazards regression. Sta-

tistical analysis was performed using the χ^2 test and multiple logistic regression.

Results: The overall rate of surgical intervention in this cohort was 34.1%. In all, 36.8% of white patients underwent surgical treatment of their disease, whereas only 19.2% of nonwhite patients did. Patients residing in areas with high poverty rates were 27% less likely to have surgery. Older age and higher comorbidity scores were also associated with lower rates of surgery. Patients who received surgical treatment for their disease experienced significantly longer survival than did patients who did not undergo surgical resection.

Conclusions: There seems to be significant underuse of esophagectomy as treatment for potentially resectable stage I, II, and III esophageal cancers across all patient groups. In nonwhite and low socioeconomic patient cohorts, the underuse is even more pronounced.

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IN 2008, 16 470 PEOPLE WILL BE diagnosed as having esophageal cancer, and 14 280 people will die of the disease.¹ Historically, esophageal cancer has carried a grim prognosis, with 5-year survival well below 25% even after surgical resection. Furthermore, short-term mortality after esophagectomy has been high (8%-25%).²⁻⁷ Many physicians and patients may, therefore, believe that the high risk of esophagectomy is not worth the short survival benefit. Accordingly, many patients with esophageal cancer never undergo surgical treatment for their disease.

See Invited Critique at end of article

Treatment of esophageal cancer has changed significantly during the past decade. Support for nonoperative treatment has increased owing to studies⁸⁻¹⁰ on the use of chemoradiation as curative treatment for

locally advanced disease. Two-year survival of 36% to 40% and 5-year survival of up to 27% have been demonstrated after chemoradiotherapy alone. On the other hand, however, improvements in surgical technique and postoperative care at high-volume hospitals have resulted in significant improvements in morbidity and mortality after esophagectomy. Several single-institution studies¹¹⁻¹⁴ have reported postesophagectomy mortality of 0.5% to 4.5%. Simultaneously, there have been reports of 5-year survival as high as 40% to 50% after esophagectomy.^{11,14} In a series of patients undergoing en bloc esophagectomy for adenocarcinoma, patients with tumors limited to the mucosa had 5-year survival after esophagectomy as high as 80%, and patients with no lymph node metastases had 5-year survival of 60%.¹⁵⁻¹⁷

The overall impact of these changes in treatment outcomes on rates of surgical resection in patients with esophageal cancer is uncertain. In one study,¹⁸ the num-

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ber of patients treated with chemoradiotherapy alone rose from 16% in 1976-1990 to 42% in 1991-1996 to 49% in 1997-2002. The purpose of this study was to determine the use of esophagectomy in individuals diagnosed as having locoregional esophageal cancer between January 1, 1997, and December 31, 2002, in the United States. We hypothesized that rates of surgery as treatment for esophageal cancer would be relatively low, particularly for minority patients residing in underprivileged communities.

METHODS

STUDY POPULATION

We obtained data from the Survival, Epidemiology, and End Results (SEER)-Medicare files (1997-2003) for patients diagnosed as having esophageal cancer between January 1, 1997, and December 31, 2002. The SEER-Medicare database brings together Medicare administrative claims data with detailed clinical tumor registry data.^{19,20} The SEER program collects data about cancer incidence, treatment, and mortality in a representative sample of the US population. The SEER coverage area, which includes 14 sites encompassing wide geographic and population variation, is estimated to include approximately 14% of the US population.^{19,21} In SEER, cancer cases are primarily identified from hospital records. Tumor characteristics, initial courses of therapy, and sociodemographic information are obtained from medical records. Except for individuals enrolled in health maintenance organizations and those who do not have Part B coverage, Medicare data provide information about all inpatient and outpatient use of medical care for residents of the United States 65 years or older. In this database, survival is determined by using Medicare vital statistics and by SEER linkage to death certificates (National Death Index), medical records, voter registration, and other public records, making it possible to assess overall and disease-specific survival.

Initially, 4123 patients were identified in the SEER database as being diagnosed as having stage I, II, or III esophageal cancer during the years of interest. We excluded 875 patients who were enrolled in a health maintenance organization during the year of their diagnosis because health maintenance organizations do not submit detailed claims to Medicare that itemize patient care. We then excluded 862 patients younger than 65 years. These patients in the Medicare data consist of individuals who are disabled or have end-stage renal disease. Because of their unusual characteristics, we did not include them in this analysis, which is a common practice when using Medicare claims data. The final study cohort was 2386 patients with stage I, II, or III esophageal cancer.

OUTCOME MEASURE

The primary outcome measure was operative intervention. Patients were identified as having surgery by the presence of an operative procedure code indicating esophagectomy in their Medicare Provider Analysis and Review (MEDPAR) files (*International Classification of Diseases, Ninth Revision*, codes 42.40, 42.41, 42.42, 42.50-42.59, 42.60-42.68, 42.90, 43.00, 43.40, 43.50, 43.99, and 42.69). Patients were categorized as being nonoperative in 2 ways. If patients had MEDPAR files that did not contain an *International Classification of Diseases, Ninth Revision*, procedure code indicating esophagectomy, they were identified as nonoperative. If patients did not have MEDPAR records, which means they had no inpatient hospitalizations, they were assumed not to have had surgery because all patients require hospitalization after esophagectomy.

PREDICTOR VARIABLES

Before data analysis, we defined the variables we believed would have a significant association with the outcome variable (surgical intervention). We proposed to study patient age, race, sex, Charlson Comorbidity Index score, socioeconomic region (SER), and tumor stage. To determine cancer stage, we used the Extent of Disease fields provided in the SEER Patient Entitlement and Diagnosis Summary File. These variables offer information regarding tumor extension and lymph nodes. Using these variables, we derived the corresponding American Joint Committee on Cancer TNM staging values and the overall cancer stage (0-IV) for each patient. As mentioned, only patients with stage I, II, or III disease were included in this study.

Patient condition was assessed using the Romano modification of the Charlson Comorbidity Index.²² The Charlson index, which has been used extensively in previous literature, uses *International Classification of Diseases, Ninth Revision*, diagnosis and procedure codes from Medicare records to give a weighted, risk-adjusted comorbidity index value per patient.²³ The Charlson index takes into consideration any comorbid conditions that meet the inclusion criteria as defined by the index variables and that occurred within a year before diagnosis. The Romano modification excludes cancer diagnoses in determining comorbidity and, thus, is used frequently in cancer outcomes research. Because of the small number of patients who received scores greater than 2, we collapsed the Romano-Charlson values into 3 categories: 0 (low; no preexisting comorbid conditions), 1 (moderate; ≥ 1 comorbid condition), and 2 or greater (high; greater number of, or more severe, comorbid conditions). This is a common practice in the surgical literature because often patients with extensive comorbid illnesses do not undergo high-risk surgical procedures.²⁴⁻²⁸

The SER was evaluated using the percentage of the population in a patient's home zip code that falls below the poverty line. We identified the median percentage below the poverty line for all patient zip codes as 8.7%. Based on this value, we defined 2 socioeconomic categories. High SERs included zip codes where 8.7% or less of the population lived below the poverty line. Low SERs included zip codes where more than 8.7% of the population lived below the poverty line.

Patient race/ethnicity was initially evaluated using 6 categories: white, black, other, Asian, Hispanic, and American Indian. Consistent with the epidemiologic pattern of esophageal cancer in the United States, most patients in the cohort were white (84.5%). Altogether, 10.2% of the patients were black, with smaller percentages being accounted for by the other racial groups. Owing to the small number of nonwhite patients, we collapsed race into 2 categories, white and nonwhite, for the purposes of statistical analysis.

SURVIVAL

We calculated survival time as the number of days from diagnosis until death or until December 31, 2003, whichever came first. We censored observations of patients who were alive at the end of follow-up.

STATISTICAL ANALYSIS

All analyses were conducted using a statistical software package (SPSS; SPSS Inc, Chicago, Illinois). Univariate analysis was performed using the χ^2 test to determine the relationship between each predictor variable described in the "Predictor Variables" section and the primary outcome. A logistic regression was used to determine which of these variables, when adjusted for possible confounders, remained a significant predic-

Table 1. Patient Characteristics and Univariate Analysis of Characteristics by Surgery Status^a

Variable	Patients, No. (%) ^b		
	No Surgery (n=1573)	Surgery (n=813)	Total (N=2386)
Age, y			
65-69	347 (56.4)	289 (43.6)	663 (27.8)
70-74	389 (58.4)	277 (41.6)	666 (27.9)
75-79	406 (71.9)	159 (28.1)	565 (23.7)
80-85	235 (78.3)	65 (21.7)	300 (12.6)
≥85	169 (88.0)	23 (12.0)	192 (8.0)
Cancer stage			
I	91 (39.4)	140 (60.6)	231 (9.7)
II	1015 (72.4)	387 (27.6)	1402 (58.8)
III	467 (62.0)	286 (38.0)	753 (31.6)
Romano-Charlson score			
0	1042 (64.1)	584 (35.9)	1626 (68.1)
1	300 (66.8)	149 (33.2)	449 (18.8)
≥2	231 (74.3)	80 (25.7)	311 (13.0)
Sex			
Male	1091 (63.4)	630 (36.6)	1721 (72.1)
Female	482 (72.5)	183 (27.5)	665 (27.9)
Race			
White	1274 (63.2)	742 (36.8)	2016 (84.5)
Nonwhite	299 (80.8)	71 (19.2)	370 (15.5)
Socioeconomic status			
High	643 (61.4)	405 (38.6)	1048 (50.0)
Low	753 (71.7)	297 (28.2)	1050 (50.0)
Unknown	177 (11.2)	111 (13.6)	288 (12.1)

^aFor all the variables, $P = .001$, χ^2 test.

^bBecause of rounding, percentages may not total 100.

tor of surgical intervention. In assessing the predictors of post-operative mortality, the variables included in the multivariate logistic model were patient age (65-69, 70-74, 75-79, 80-84, and ≥85 years), race (white and nonwhite), sex (male and female), SER (upper and lower), Romano-Charlson score (0, 1, and ≥2), and tumor stage (I, II, and III).

For survival analysis, we constructed Kaplan-Meier curves and compared them using the log-rank test. We used Cox proportional hazards models to examine the relationship between surgical status and mortality, adjusting for patient characteristics, including age, comorbidity score, race, SER, and tumor stage.

RESULTS

COHORT CHARACTERISTICS

We identified 2386 patients in the SEER-Medicare files who had stage I, II, or III esophageal cancer diagnosed between January 1, 1997, and December 31, 2002 (**Table 1**). The mean age of patients in this cohort was 74 years. Consistent with the known patterns of esophageal cancer incidence, most patients were male and white. Also, most patients had stage II (58.8%) or III (31.6%) disease at diagnosis; only 9.7% had stage I disease. The Romano-Charlson scores for the cohort overall were low, with 68.1% of patients having a Romano-Charlson score of 0.

SURGICAL INTERVENTION

The overall rate of esophagectomy was 34.1% (n=813). Univariate analysis revealed that single factors signifi-

Table 2. Predictors of Surgical Intervention by Multivariate Analysis

Variable	β Coefficient	Odds Ratio	P Value
Age, y			
65-69	0	1 [Reference]	
70-74	-0.07	0.93	.52
75-79	-0.69	0.50	<.001
80-84	-0.98	0.37	<.001
≥85	-1.6	0.19	<.001
Cancer stage			
I	0	1 [Reference]	
II	-1.27	0.29	<.001
III	-0.93	0.39	<.001
Romano-Charlson score			
0	0	1 [Reference]	
1	-0.04	0.96	.71
≥2	-0.41	0.67	.006
Sex			
Male	0	1 [Reference]	
Female	-0.27	0.77	.01
Race			
Nonwhite	0	1 [Reference]	
White	0.87	2.39	<.001
Socioeconomic status			
High	0	1 [Reference]	
Low	-0.32	0.73	.002

cantly associated with surgical intervention included patient age, Romano-Charlson score, sex, race, SER, and tumor stage (Table 1).

The results of logistic regression are given in **Table 2**. All the variables in the regression remained significant independent predictors of surgical intervention when adjusted for the other variables in the model. Increasing age was highly associated with decreased odds of surgical intervention. The odds of surgical intervention in patients aged 75 to 79 years were half those of patients aged 65 to 74 years ($P < .001$). Similarly, patients with Romano-Charlson scores of 2 or greater were two-thirds as likely to receive surgical treatment for their disease as were patients with more minimal comorbidities ($P = .006$). Although stage II and III disease are amenable to surgery, patients with these more advanced cancers were treated surgically much less often than were those with early-stage disease (stage II: odds ratio, 0.29; $P < .001$ and stage III: 0.39; $P < .001$). Men were 23% more likely to receive surgery for their disease than were women ($P = .01$). Both SER and race significantly affected the rate of surgical intervention. Patients residing in high-poverty areas had 27% lower odds of undergoing surgery than patients in regions with lower poverty rates. In addition, race was strongly associated with use of surgery. The odds of a white patient receiving surgery for their disease were more than 2 times those of a nonwhite patient when adjusted for all other independent variables ($P < .001$).

Using the results of logistic regression, the probability of surgical intervention for a variety of patient types was determined (**Table 3**). A 68-year-old white man who has no comorbid conditions, lives in a high socioeconomic area, and has stage I disease has a 76% probability of receiving surgical treatment for his disease. A non-

white patient with those same characteristics, including stage I disease, has only a 57% likelihood of undergoing surgical treatment. For the same patients with stage II disease, the probability of surgery is only 47% and 27% (white and nonwhite, respectively). In general, non-white patients were 20% less likely to receive surgery than were white patients.

SURVIVAL

Patients who underwent surgical resection had significantly longer survival compared with patients who did not have surgery (**Figure**). Median time of survival from date of diagnosis was 620 days for surgical patients and 381 days for patients not receiving surgery. Two-year survival was 46.9% and 32.3% for surgery and nonsurgery patients, respectively. Similarly, 5-year survival for the 2 groups was 28% and 10%, respectively. When adjusted for patient and tumor characteristics, including age, comorbidity burden, SER, race, and tumor stage, surgical resection remained significantly associated with greater long-term survival (hazard ratio, 0.69; $P < .001$).

COMMENT

These results indicate that rates of surgical intervention for the treatment of esophageal cancer are low. Although all the patients in this cohort had potentially resectable stage I, II, or III disease, the overall surgery rate was only 34.1%. In stage I disease, in which resection has been associated with up to 80% long-term survival, only 60.6% of patients underwent surgery. Furthermore, certain demographic subgroups had particularly low rates of surgery. Whereas the overall surgery rate was 36.8% in white patients, it was only 19.2% in nonwhite patients. Similarly, the rates of surgical intervention were 38.6% and 28.3% for patients living in areas with lower and higher poverty rates, respectively.

There is little controversy regarding appropriate therapy for stage I esophageal cancer. Surgery is the primary curative therapy for medically fit patients with this stage of disease. However, in this cohort, only 60.6% of all patients with stage I disease and only 39.1% of nonwhite patients with stage I disease underwent surgical resection. There was no difference in the age or comorbidity status of white and nonwhite patients with stage I disease; in fact, the mean age of stage I white patients was more than 1 year greater than that of nonwhite patients. These data highlight a baseline underuse of surgery in this population that is even more striking in nonwhite patients.

There has been more controversy in the literature regarding appropriate treatment of stage II and III esophageal cancers. In general, these are still considered resectable diseases. The current debate has, for the most part, centered on the efficacy of neoadjuvant chemoradiotherapy before surgery vs surgical treatment alone. However, more recently, 2 randomized controlled trials^{10,29} comparing chemoradiotherapy alone with chemoradiation and surgery for stage II and III esophageal cancers found that long-term survival was equivalent in the 2 arms.

Table 3. Probability of Surgery by Cancer Stage, Age Group, and Race Category^a

Cancer Stage and Age Group	P Value	
	White	Nonwhite
Stage I		
65-69 y	.76	.57
70-74 y	.75	.55
75-79 y	.61	.39
80-84 y	.54	.33
≥85 y	.37	.19
Stage II		
65-69 y	.47	.27
70-74 y	.45	.25
75-79 y	.31	.15
80-84 y	.25	.12
≥85 y	.14	.06
Stage III		
65-69 y	.56	.34
70-74 y	.54	.32
75-79 y	.39	.21
80-84 y	.32	.16
≥85 y	.19	.09

^aAll other categories assigned baseline category (highest probability of surgery): male, upper socioeconomic region, and Romano-Charlson score of 0.

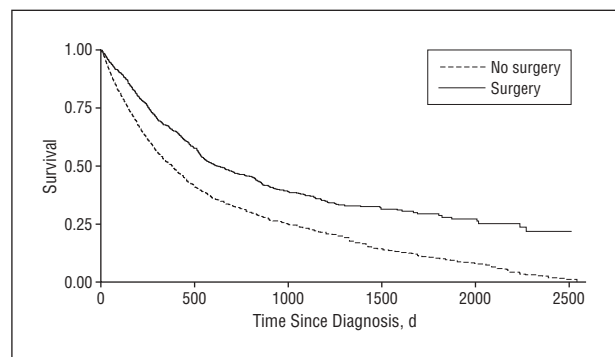


Figure. Kaplan-Meier survival curves by surgical status. These curves differ significantly (log-rank test $P < .001$).

Proponents of nonsurgical therapy for stage II and III esophageal cancers rely on these results to support their decision. The surgical mortality in both of these trials, however, exceeded 10%, which is much higher than recent mortality rates reported by high-volume surgical centers (0.5%-4%).¹¹⁻¹⁴ The 2007 National Comprehensive Cancer Network esophageal guidelines mention these trials and conclude that their surgical mortality was too high to make any true comparison regarding survival between the 2 treatment strategies.³⁰ Thus, the evidence is currently insufficient to support the use of chemoradiotherapy alone as standard therapy for locally advanced stage II and III esophageal cancers.

Despite the National Comprehensive Cancer Network guidelines and limited evidence supporting nonoperative treatment for stage II and III esophageal cancers, these data suggest that the rate of surgical therapy in stage II and III patients is low. In this cohort, only 27.7% of stage II and 38.0% of stage III patients underwent esophageal resection. Again, lower rates of surgical interven-

tion were observed for nonwhite patients and those living in low SERs (Table 3).

The racial inequality observed herein is consistent with many other published studies³¹⁻³⁵ documenting racial and socioeconomic disparity in treatment patterns for malignant neoplasms. In all of these studies, patient factors, such as SER, age, and comorbidity score, do not explain the disparate rate of surgery between white and nonwhite patients. There are currently many ongoing investigations studying the possible causes of the racial variations in treatment patterns. Historically, it was believed that the lower rates of surgical intervention as cancer treatment in minority populations were due to provider bias, unequal access to health care, and higher comorbidity burden in the minority population.^{31,36,37} More recently, however, there is evidence that lower rates of surgical intervention in nonwhite patients may be partially explained by suboptimal patient-physician interactions and patient preference.^{38,39} Several recent studies^{32,40,41} looking at racial disparities in the treatment of esophageal cancer reported similar disparities to those found in this study. Additional work needs to be done to identify provider and patient characteristics that result in underuse of care and to implement strategies to overcome these barriers.

This study has several limitations. First, there is always the possibility of misclassification of surgical status or SER when using administrative claims data. The SEER data, however, have been well validated for studying cancer surgery outcomes and have been used in numerous such studies.^{19,42} Also, in restricting the study population to patients 65 years or older, we limited the generalizability of these findings. Although rates of surgical intervention in younger patients might be higher, this does not diminish the fact that in this cohort, only 34.1% of patients with potentially resectable disease received surgical treatment. Another significant limitation of this data set is that we could not determine whether a patient was offered surgery but refused. It is possible that surgical therapy is recommended by physicians at a higher rate than we see by looking at the actual rate of resection. A recent study⁴³ evaluating the rate of pancreatic resection for stage I pancreatic cancer identified patients who were offered but refused surgery. The rate of surgery as a recommended treatment was still very low in this cohort, especially in the nonwhite patient population.⁴³ Future studies are needed to investigate the role of provider bias and patient beliefs in treatment disparity for esophageal and other cancers.

Finally, we recommend caution when interpreting the survival data. Although we adjusted for many patient-level factors (age, Romano-Charlson score, race, etc) that might affect the decision to undergo major cancer surgery, we could not completely eliminate the potential for selection bias when comparing surgical and nonsurgical patient outcomes.

Overall, esophagectomy seems to be grossly underused as a treatment for patients with stage I, II, and III esophageal cancers. Refinements in operative technique and postoperative care have allowed resection to be performed with greater safety. In addition, in select patients, surgery is associated with improved long-term survival. Recently, there have been reports of 5-year survival as high

as 35% to 80% after esophagectomy.^{11,14,16,17} It is imperative that physicians diagnosing and treating patients with esophageal cancer be made aware of the positive progress in the surgical treatment of this disease. They can use this information to educate and to more appropriately recommend surgery to their patients with cancer.

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INVITED CRITIQUE

Paulson and associates analyzed the SEER database to characterize the use of esophagectomy for patients with a diagnosis of esophageal cancer. Their findings suggest that, despite data establishing surgical resection as the treatment of choice for stage I disease, fewer patients than expected underwent esophagectomy, and these differences were particularly significant for nonwhite patients and those from regions with higher poverty rates. The nonoperative group included patients primarily treated with chemotherapy and/or radiotherapy and those who refused all treatment, so the meaning of the outcome comparisons is difficult to determine. It also seems likely that underuse rates are greater for the SEER population 65 years or older than they would be for all patients because of comorbidities.

Despite these limitations, these findings add to a growing body of literature suggesting underuse of and disparities in surgical care, particularly for highly lethal malignant neoplasms. The explanations are multiple and include nihilism on the part of physicians and patients, referral to oncologists vs surgeons, and differences in access to care. In addition, there is growing evidence that cultural differences and racial

and economic biases, in both patients and providers, play a significant role.

Addressing such underuse and disparities is clearly a mandate for our profession. Not only must we educate patients and referring physicians as to the possible treatment options available but we also must strive to facilitate better access through open multidisciplinary forums, such as tumor boards. In addition, cultural competence, to ensure that treatment decisions are not based on ill-defined perceptions of age, race, sex, or economic resources, needs to become a priority in our training programs and a part of continuing certification. There is every reason to believe that such efforts will have as big an effect on overall outcomes as any advances in the therapy of these diseases.

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