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ORIGINAL ARTICLE

Survival Disparities by Race and Ethnicity in Early Esophageal Cancer

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Abstract

Background Survival outcome disparities among esophageal cancer patients exist, but are not fully understood.

Aims We used the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database to determine whether survival differences among racial/ethnic patient populations persist after adjusting for demographic and clinical characteristics.

Methods Our study included T1-3N0M0 adenocarcinoma and squamous cell cancer patients diagnosed between 2003 and 2011. We compared survival among two racial/ethnic patient subgroups using Cox proportional hazards methods, adjusting for age, sex, histology, marital status, socioeconomics, SEER region, comorbidities, T stage, tumor location, diagnosis year, and treatment received.

Results Among 2025 patients, 87.9% were White and 12.1% were Nonwhite. Median survival was 18.7 months for Whites vs 13.8 months for Nonwhites ($p = 0.01$). In the unadjusted model, Nonwhite patients had higher risk of mortality (HR = 1.29, 95% CI 1.11–1.49, $p < 0.0001$) when compared to White patients; however, in the Cox regression adjusted model there was no significant difference (HR = 0.94, 95% CI 0.80–1.10, $p = 0.44$). Surgery, chemotherapy, younger age, lower T stage, and lower Charlson comorbidity score were significant predictors in the full adjusted model.

Conclusions Differences in mortality risk by race/ethnicity appear to be largely explained by additional factors. In particular, associations were seen in surgery and T stage. Further research is needed to understand potential mechanisms underlying the differences and to better target patients who can benefit from treatment options.

Keywords Esophageal cancer · Disparities · SEER-Medicare · Outcomes · Survival

Introduction

Esophageal cancer incidence in the USA has risen over the past 20 years, with an estimated 16,940 new cases and 15,690 deaths expected in 2017 [1, 2]. The incidence of esophageal adenocarcinoma, which is predominately diagnosed in White patients, has risen dramatically, while squamous cell carcinoma, which is more commonly diagnosed in Black patients, has decreased [3, 4].

Despite advancements in treatment options for patients with esophageal cancer, overall survival remains poor, with a five-year survival of less than 20% [1]. Approximately 20% of esophageal cancer is found at the localized stage (T1-3, N0, M0), and five-year survival among this population is 43% [5]. However, Black patients have a five-year survival rate of 23%, a substantially smaller proportion compared with White patients, who have a five-year survival rate of 45%. Thus, this suggests a clear disparity in survival outcomes by race. Although differences in biology

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may play a role in these racial survival disparities, variation in the receipt of certain treatment options and access to health care is thought to explain these differences [6, 7]. Prior studies involving patients with esophageal and other cancer types have shown that race/ethnicity are predictors of whether patients receive cancer-directed surgery [7–10]. Potential explanations for the lower likelihood that racial minorities receive cancer-directed surgery have included theories suggesting that these patients' lower socioeconomic status, higher comorbidities, and decreased access to care are involved [11].

While earlier studies have suggested that disparities no longer persist after adjusting for treatment receipt [6, 12, 13], they largely focused on registry data, which do not always contain important variables, such as comorbid medical conditions and complete treatment information. Therefore, in the current study, we used the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database to determine whether these racial/ethnic differences in overall and cancer-specific survival outcomes persist after controlling for important confounders, such as patients' sociodemographic and clinical characteristics.

Methods

Cohort Inclusion/Exclusion Criteria

We identified adenocarcinoma and squamous cell cancer patients diagnosed between 2003 and 2011 from the 2015 release of the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute and Medicare linked data, using International Classification of Diseases for Oncology (ICD-O-3) codes as outlined in Table 1. The SEER database includes cancer incidence and survival data collected from cancer registries covering about 28% of the US population. The Medicare database includes information for approximately 97% of patients aged 65 and older who receive Medicare benefits in the USA. The SEER-Medicare data link SEER to Medicare enrollment and claim files maintained by the Center for Medicare and Medicaid Services, including Parts A and B claims for covered healthcare services. We included patients who were diagnosed with a non-metastatic primary cancer at age 66 or above between January 1, 2003, and December 31, 2011, that was pathologically confirmed. To ensure that we captured complete claims data for each patient, we included only those with continuous enrollment in Medicare Parts A and B from 13 months before diagnosis (for Charlson comorbidity score estimation) until death or December 31, 2013, whichever came first, and who were not enrolled in an HMO (for treatment information). We determined T, N, and M stage according to the AJCC 7th edition per the Collaborative Stage Data Collection System Version 02.05 using SEER variables for tumor extension, lymph nodes, and metastasis, respectively. We included patients who had T1-3, N0, M0 tumors to focus on early-stage cancer who are most likely to receive treatment, including surgery.

We estimated the comorbidity score by applying the Deyo et al. adaptation of the Charlson comorbidity index, which allows for index scores from ICD-9 diagnosis and procedure codes to Medicare inpatient, outpatient, and physician claims during the 13-month period prior to cancer diagnosis and classified patients into the groups based on the presence of 0, 1, or 2 + comorbid conditions [14–17]. We calculated an ecological socioeconomic status by using US Census data provided in SEER-Medicare to derive quintiles of ZIP code-level median household income. We categorized patients into two race/ethnicity groups (White, Nonwhite [Black, Hispanic, Asian]) using SEER variables; we excluded < 11

Table 1 SEER-Medicare claims codes

Variable	Source	Codes
Adenocarcinoma diagnosis	ICD-0-3 codes	8050, 8140-8147, 8160-8162, 8180-8221, 8250-8507, 8514, 8520-8551, 8560, 8570-8574, 8576, 8940-8941
Squamous cell carcinoma diagnosis	ICD-0-3 codes	8070-8078, 8083, 8084
Surgery	CPT or ICD-9 Procedure Codes	43100, 43101, 43107, 43108, 43112, 43113, 43116, 43117, 43118, 43119, 43121, 43122, 43123, 43124, 43217, 43216, 43228, 43250, 43251, 43257, 43258, 96570, 96571, 42.33
Radiation	CPT or ICD-9 Procedure Codes	ICD-9-CM: V58.0, 92.21-92.29 CPT: 7331-7336, 73399, 77400-77499, 77750-77799 Revenue Center: 0330, 0333, 0339
Chemotherapy	CPT or ICD-9 Procedure Codes	ICD-9-CM: V58.1, 99.25 HCPCS: C1166, C1168, C1179, C9110, C9205, C9207, C9213-C9216, C9411, C9414-C9419, C942x, C9430-C9438, G0345-G0363, J9000–J9999, Q0083–Q0085 CPT: 9651x-9654x, 964xx Revenue Center 0331, 0332, 0335

patients with other or unknown race. We defined treatment variables based on the CPT and ICD-9 codes listed in Table 1; we included local endoscopic treatment in the surgery variable. We determined the cause of death using SEER data.

Statistical Analysis

Our primary outcomes of interest were overall and cancer-specific survival among the racial/ethnic subgroups. We evaluated differences in the distribution of baseline characteristics between these groups using Chi-square tests. We plotted overall and cancer-specific survival using Kaplan–Meier curves. We constructed a Cox proportional hazard model to examine factors contributing to the survival differences across groups. We defined survival as the time from the date of diagnosis to the date of death or December 31, 2013, whichever came first. We estimated the hazard ratio before adjustment and then after adjustment for a select number of potential confounders: age at diagnosis (66–69, 70–74, 75–79, 80–84, 85 +); sex; race and ethnicity; year of diagnosis (2003–2005, 2006–2018, 2009–2011); SEER region; marital status; median income (census tract quintile); histology (adenocarcinoma, squamous cell); T stage; tumor location (lower, middle, upper); Charlson comorbidity score; and treatment (surgery/local therapy, radiation, chemotherapy). We analyzed the adjusted model without treatment and again with treatment (surgery/endoscopic therapy, radiation, or chemotherapy) included. We defined statistical significance as p value < 0.05 in a two-sided test. We performed all statistical analyses using SAS software, version 9.4 (SAS Institute, Inc).

Results

Patient Characteristics

The final cohort included 2025 patients; 1779 (88%) were White, and 246 (12.1%) were Nonwhite. Among the Nonwhite group, 152 (61.8%) were Black, 68 (27.6%) were Asian, and 27 (11.0%) were Hispanic. Nonwhite patients were more likely to be female, unmarried, diagnosed in earlier years, from the South or West/Hawaii, have a lower SES (census tract quintile), or receive radiation compared to White patients. White patients were more likely to have adenocarcinoma or a tumor in the lower esophagus, while Nonwhite patients were more likely to have a squamous cell cancer or tumor in the middle esophagus. White patients were more likely to receive surgery compared to Nonwhites (46.4% vs 28.4%). We observed no statistically significant differences in age, AJCC stage, Charlson comorbidity score, or chemotherapy receipt between the two groups. The full list of patient characteristics is listed in Table 2.

Survival Trends and Outcomes

Figure 1 displays the Kaplan–Meier curves for overall and cancer-specific survival, stratified by race/ethnicity. The median (25th, 75th percentile) survival for the entire cohort was 17.6 months (6.2, 42.1). The median (25th, 75th percentile) survival was 18.7 months (6.2, 43.6) and 13.8 months (5.9, 32.0) for White and Nonwhite patients, respectively ($p = 0.01$).

Figure 2 displays the Kaplan–Meier curves for overall and cancer-specific survival, stratified by surgery receipt and race/ethnicity. Among patients who received surgery, the median (25th, 75th percentile) survival was 36.8 months (17.8, 66.8) and 31.8 months (16.4, 53.6) for White and Nonwhite patients, respectively ($p = 0.06$). Among patients who did not receive surgery, the median (25th, 75th percentile) survival was 9.5 months (3.8, 22.8) and 8.1 months (4.0, 21.2) for White and Nonwhite patients, respectively ($p = 0.80$).

In the unadjusted Cox proportional hazards models, Nonwhite patients had higher hazards for mortality in the overall (HR 1.29, 95% CI 1.11–1.49, $p = 0.0006$) and cancer-specific models (HR 1.36, 95% CI 1.15–1.60, $p = 0.0003$) compared with White patients. These were no longer statistically significant when adjusted for all variables except treatment (HR 1.001, 95% CI 0.85–1.18, $p = 0.99$ and HR 1.00, 95% CI 0.83–1.20, $p = 0.99$) for overall and cancer-specific models, respectively). We found similar results with the addition of the treatment variables (surgery, radiation, chemotherapy) in the models comparing Nonwhite and White patients (HR 0.94 95% CI 0.80–1.10, $p = 0.44$ and HR 0.93, 95% CI 0.77–1.12, $p = 0.45$) for overall and cancer-specific models, respectively).

Surgery had a significant association in the full adjusted model, with patients who received surgery having lower hazards for mortality when compared to those who did not receive surgery, with HR 0.36 (95% CI 0.32–0.41, $p < 0.0001$) and HR 0.31 (95% CI 0.27–0.36, $p < 0.0001$) for overall and cancer-specific models, respectively. Chemotherapy receipt also was associated with a lower hazard for mortality in the overall (HR 0.82, 95% CI 0.72–0.93, $p = 0.002$) and cancer-specific models (HR 0.79, 95% CI 0.68–0.91, $p = 0.002$). A Charlson comorbidity score of 2 or higher predicted worse outcomes in both models, with HR 1.51 (95% CI 1.34–1.70, $p < 0.0001$) and HR 1.35 (95% CI 1.06–1.42, $p = 0.006$) for overall and cancer-specific models, respectively, when compared to a Charlson score of 0. Older patient subgroups had a higher hazard for mortality compared with ages 66–69 in the adjusted overall model (HR 1.29, 95% CI 1.09–1.53, $p = 0.003$ for 75–79; HR 1.37,

Table 2 Patient characteristics (T1-3N0M0)

Characteristic	White ($N=1779$)	Nonwhite ($N=246$)	p value
Age			
66–69	320 (18.0%)	40 (16.3%)	0.25
70–74	407 (22.9%)	67 (27.2%)	
75–79	414 (23.3%)	63 (25.6%)	
80–84	348 (19.6%)	47 (19.1%)	
85+	290 (16.3%)	29 (11.8%)	
Age (Mean, SD)	76.9 (7.1)	75.1 (6.5)	
Sex			
Male	1266 (72.2%)	160 (65.0%)	0.049
Female	513 (28.8%)	86 (35.0%)	
Marital status			
Unmarried	648 (36.4%)	133 (54.1%)	< 0.0001
Married	1038 (58.4%)	*	
Unknown	93 (5.2%)	*	
Year of diagnosis			
2003–2005	611 (34.5%)	103 (41.9%)	0.03
2006–2008	608 (34.2%)	83 (33.7%)	
2009–2011	560 (31.5%)	60 (24.4%)	
SEER region			
Northeast	406 (22.8%)	32 (13.0%)	0.0001
South	427 (24.0%)	80 (32.5%)	
Midwest	243 (13.7%)	23 (9.4%)	
West/Hawaii	703 (39.5%)	111 (45.1%)	
SES**			
0 (lowest)	240 (13.5%)	104 (42.3%)	< 0.0001
1	337 (18.9%)	48 (19.5%)	
2	361 (20.3%)	38 (15.5%)	
3	415 (23.3%)	34 (13.8%)	
4 (highest)	426 (24.0%)	22 (8.9%)	
Histology			
Adenocarcinoma	1220 (68.6%)	54 (22.0%)	< 0.0001
Squamous cell carcinoma	559 (31.4%)	192 (78.15%)	
Stage			
I	1098 (61.7%)	154 (62.6%)	0.79
II	681 (38.3%)	92 (37.4%)	
T stage			
T1a	369 (20.7%)	29 (11.8%)	< 0.0001
T1b	166 (9.3%)	14 (6.7%)	
T1NOS	563 (31.7%)	111 (45.1%)	
T2	286 (16.1%)	41 (16.7%)	
T3	395 (22.2%)	51 (20.7%)	
Charlson score			
0	745 (41.9%)	105 (42.7%)	0.83
1	502 (28.2%)	65 (26.4%)	
2+	532 (29.9%)	76 (26.4%)	
Esophagus location			
Lower	1092 (61.4%)	83 (33.7%)	<0.0001
Middle	375 (21.1%)	107 (43.5%)	
Upper	123 (6.9%)	23 (9.4%)	
Unknown	189 (10.6%)	33 (13.4%)	
Surgery			

Table 2 (continued)

Characteristic	White ($N=1779$)	Nonwhite ($N=246$)	p value
No	953 (53.6%)	176 (71.5%)	< 0.0001
Yes	826 (46.4%)	70 (28.4%)	
Radiation			
No	724 (40.7%)	79 (32.1%)	0.01
Yes	1055 (59.3%)	167 (67.9%)	
Chemotherapy			
No	938 (52.7%)	146 (59.4%)	0.051
Yes	841 (47.3%)	100 (40.7%)	

*Values suppressed in accordance with SEER-Medicare guidelines to mask cell sizes that may be < 11 and ensure patient confidentiality. Percentages may not add to 100 due to rounding

**SES: quintiles based on median income by census tract ZIP code

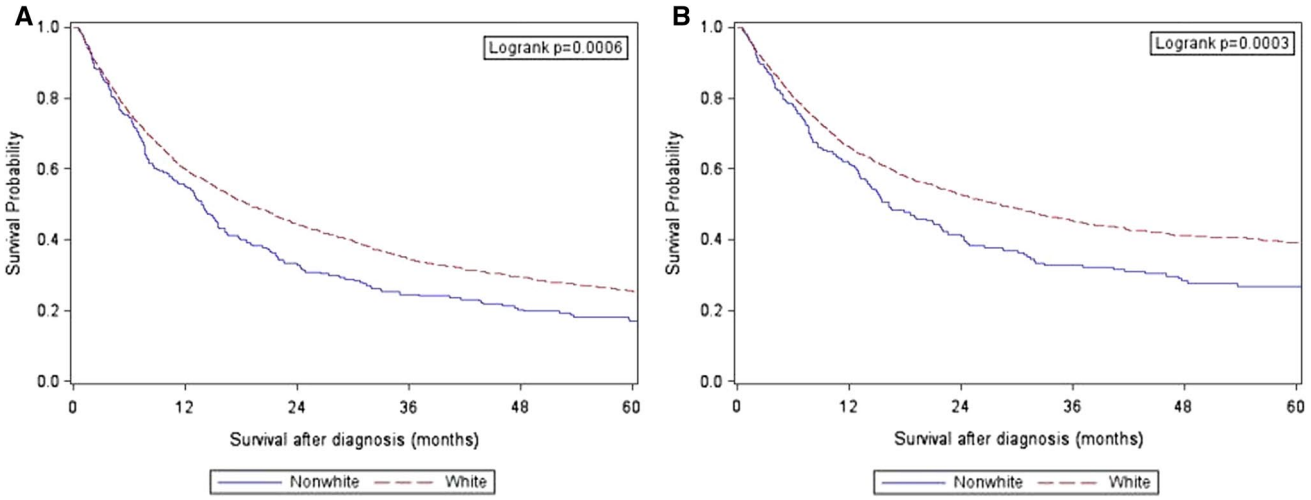

Fig. 1 Overall (**a**) and cancer-specific (**b**) survival by race/ethnicity

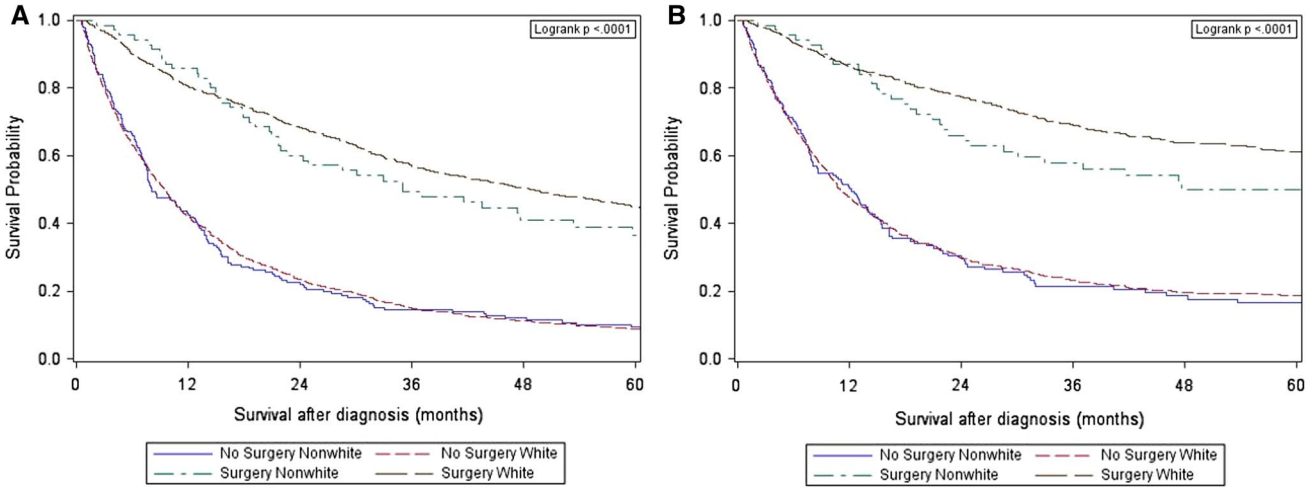

Fig. 2 Overall (**a**) and cancer-specific (**b**) survival by race/ethnicity and surgery receipt

95% CI 1.15–163, $p = 0.0005$ for 80–84; HR 1.89, 95% CI 1.57–2.27, $p < 0.0001$ for 85 +); similar results were found in the cancer-specific model. Sex, SES, histology, and receipt of radiation were not significant in either model. Full results are found in Table 3.

Discussion

We analyzed data from the SEER-Medicare linked database and demonstrated the presence of racial/ethnic survival disparities among patients with localized esophageal cancer. Importantly, we found that these disparities no longer persisted after controlling for key demographic and clinical characteristics. Treatment received, such as surgery, and chemotherapy were strongly associated with differences in survival outcomes across races. Notably, White patients were more likely to receive surgery than Nonwhite patients (Table 2). While the Kaplan–Meier curve showed poorer survival among Nonwhites compared to Whites, when stratified into four groups, survival appeared to be largely driven by surgery rather than racial/ethnic group (Fig. 2). Thus, our findings suggest that racial disparities in survival among patients with localized esophageal cancer may be partially explained by the disparities in treatment received.

T stage, which represents tumor depth invasion into the esophagus, was also strongly associated with differences in survival outcomes. This is comparable to an earlier study, which demonstrated that patients with a higher T stage had poorer prognosis, independent of other factors [18]. White patients were more likely to have T1a cancers, while T3 cancers were comparable among Whites and Nonwhites, and Nonwhites were more likely to be T1NOS (Table 2). Previous studies have shown that Black patients present with esophageal cancer at later stages than White patients [6, 13, 19]. It is possible that among localized cancer patients, Nonwhites still present later than White patients. This result highlights the need for further research in this area.

Our results are consistent with several prior studies analyzing disparities among esophageal cancer patients within the SEER database [12, 20]. An earlier SEER-Medicare study also demonstrated that Black patients diagnosed with locoregional esophageal cancer in 1991–1999 had lower rates of surgical receipt when compared to White patients [21]. Survival rates in this study were lower among Blacks, but this difference did not persist when adjusting for treatment, suggesting that underuse of surgery is a major factor for worse survival in this population. Lower rates of surgery among Black patients may be explained by factors such as barriers to care, patient preferences, and low patient–physician interactions, which could explain the differences seen [9, 22]. Importantly, our study of more current data demonstrates that these treatment disparities still exist, and our findings underscore the need to better understand potential barriers to surgery.

Our study has several strengths. First, we used the SEER-Medicare linked database, which contains a large number of patients and allowed us to include additional variables, such as chemotherapy receipt, Charlson comorbidity score, and ecological SES when analyzing more recent years. Prior studies have been largely based on SEER and other registries that lacked the information available to study the potential importance of these variables. Our study also has several limitations. SEER-Medicare mainly includes patients 65 years or older, and thus, we cannot generalize our findings to younger populations. However, esophageal cancer is more common among older age-groups, with approximately 60% of patients diagnosed at age 65 or older. The number of Hispanic and Asian patients was too small to be included as their own subgroups. To date, few studies have investigated disparities among Hispanic and Asian patients with esophageal cancer [12, 13]. Thus, additional research that focused on disparities among Hispanic and Asian patients is warranted.

In addition, we lack information about access to treatment facilities and specialists, as well as data regarding patient–physician communication, and these are all factors that could influence treatment decision making for patients with esophageal cancer. Medicare claims data do not completely and accurately capture behavioral factors, such as smoking and alcohol use, which are known risk factors for squamous cell cancer and may influence both treatment decisions and survival outcomes [23–25].

In conclusion, our results suggest that race/ethnicity disparities in overall or cancer-specific survival in localized esophageal cancer may be explained by demographic, clinical, and treatment variables. Notably, T stage, surgery, and chemotherapy were strongly associated with survival differences, suggesting the presence of treatment disparities between Nonwhite and White patients confound their survival outcomes. Further research is needed to understand the causes of these differences and to better target patients who can benefit from specific treatment options, such as surgery.

Table 3 Cox proportional hazard ratios for overall and cancer-specific mortality after adjustment for patient and tumor characteristics

Characteristic	Overall		Cancer-specific	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
Race/ethnicity				
Unadjusted model				
White	1.0 (Ref)		1.0 (Ref)	
Nonwhite	1.29 (1.11–1.49)	0.0006	1.36 (1.15–1.60)	0.0003
Adjusted model (no treatment)*				
White	1.0 (Ref)		1.0 (Ref)	
Nonwhite	1.001 (0.85–1.18)	0.99	1.00 (0.83–1.20)	0.99
Adjusted model (including treatment)**				
Race/ethnicity				
White	1.0 (Ref)		1.0 (Ref)	
Nonwhite	0.94 (0.80–1.10)	0.44	0.93 (0.77–1.12)	0.45
Age at diagnosis				
66–69	1.0 (Ref)		1.0 (Ref)	
70–74	1.10 (0.93–1.30)	0.29	1.08 (0.88–1.33)	0.46
75–79	1.29 (1.09–1.53)	0.003	1.29 (1.06–1.58)	0.01
80–84	1.37 (1.15–1.63)	0.0005	1.24 (1.01–1.53)	0.04
85+	1.89 (1.57–2.27)	< 0.0001	1.76 (1.42–2.19)	< 0.0001
Sex				
Male	1.0 (Ref)		1.0 (Ref)	
Female	0.54 (0.84–1.07)	0.41	1.04 (0.90–1.19)	0.62
Marital status				
Unmarried	1.0 (Ref)		1.0 (Ref)	
Married	0.77 (0.69–0.86)	< 0.0001	0.79 (0.69–0.90)	0.0004
Unknown	0.70 (0.55–0.90)	0.005	0.66 (0.49–0.90)	0.008
Year of diagnosis				
2003–2005	1.0 (Ref)		1.0 (Ref)	
2006–2008	1.06 (0.94–1.19)	0.37	0.99 (0.87–1.14)	0.93
2009–2011	0.89 (0.78–1.01)	0.09	0.79 (0.68–0.92)	0.002
SEER region				
Northeast	1.0 (Ref)		1.0 (Ref)	
South	1.45 (1.24–1.70)	< 0.0001	1.40 (1.16–1.69)	0.0004
Midwest	1.18 (0.94–1.36)	0.16	0.96 (0.77–1.20)	0.73
West/Hawaii	1.11 (0.96–1.27)	0.16	1.11 (0.94–1.31)	0.22
SES				
0 (lowest)	1.0 (Ref)		1.0 (Ref)	
1	0.95 (0.80–1.11)	0.50	0.93 (0.76–1.13)	0.47
2	0.88 (0.75–1.04)	0.13	0.88 (0.73–1.08)	0.23
3	0.88 (0.75–1.03)	0.12	0.92 (0.77–1.12)	0.41
4 (highest)	0.91 (0.77–1.08)	0.27	0.90 (0.73–1.08)	0.23
Histology				
Adenocarcinoma	1.0 (Ref)		1.0 (Ref)	
Squamous cell carcinoma	0.96 (0.84–1.09)	0.50	0.93 (0.79–1.09)	0.35
T stage				
1a	1.0 (Ref)		1.0 (Ref)	
1b	1.15 (0.83–1.31)	0.21	1.21 (0.90–1.61)	0.20
1NOS	1.51 (1.22–1.69)	< 0.0001	1.70 (1.39–2.08)	< 0.0001
2	1.25 (0.97–1.41)	0.02	1.39 (1.10–1.74)	0.005
3	1.78 (1.35–1.92)	< 0.0001	1.97 (1.59–2.43)	< 0.0001

Table 3 (continued)

Characteristic	Overall		Cancer-specific	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
Charlson score				
0	1.0 (Ref)		1.0 (Ref)	
1	1.09 (0.96–1.23)	0.18	1.01 (0.87–1.16)	0.93
2+	1.51 (1.34–1.70)	< 0.0001	1.35 (1.06–1.42)	0.006
Esophagus location				
Lower	1.0 (Ref)		1.0 (Ref)	
Middle	0.96 (0.83–1.10)	0.52	0.91 (0.78–1.07)	0.27
Upper	0.71 (0.57–0.88)	0.002	0.71 (0.55–0.91)	0.006
Unknown	1.10 (0.93–1.30)	0.27	1.04 (0.86–1.27)	0.67
Surgery				
No	1.0 (Ref)		1.0 (Ref)	
Yes	0.36 (0.32–0.41)	< 0.0001	0.31 (0.27–0.36)	< 0.0001
Radiation				
No	1.0 (Ref)		1.0 (Ref)	
Yes	0.89 (0.77–1.02)	0.10	0.88 (0.75–1.04)	0.10
Chemotherapy				
No	1.0 (Ref)		1.0 (Ref)	
Yes	0.82 (0.72–0.93)	0.002	0.79 (0.68–0.91)	0.002

*Race/ethnicity HRs based on overall and cancer-specific adjusted models without treatment

**HRs for race/ethnicity and all other covariates based on full adjusted models, with treatment

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Compliance with ethical standards

Conflict of interest There are no conflicts of interest to disclose.

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