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Racial Disparities in Esophageal Cancer Survival After Surgery

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Objectives: Esophageal cancer (EC) black patients have higher mortality rates than Whites. The lower rate of surgery in Blacks may explain the survival difference. We explored the Surveillance Epidemiology and End Results database to determine the impact of surgery on mortality in Blacks and Whites EC.

Methods: All cases of pathologically proven local and locoregional adenocarcinoma and squamous cell carcinoma of the esophagus from 1973 to 2011 were identified (13,678 White, 2,894 Black patients). Cervical esophageal cancer was excluded. Age, sex, diagnosis year, stage, cancer-directed surgery, radiation, and vital status were analyzed according to self-reported race.

Results: Blacks had higher 1-year mortality, adjusted for age, sex, stage, year of diagnosis, histology, and therapy [adjusted hazard ratio (HR_{adj}): 1.24 (95% CI 1.16–1.32)]. Undergoing surgery was an independent predictor of improved survival overall (HR_{adj} 0.30, 95% CI 0.27–0.33). Black patients treated surgically experienced significantly lower survival than Whites, but the difference was not observed in those who did not undergo surgery.

Conclusions: Although surgery appears to reduce mortality overall, early survival is worse for Blacks. Investigation into racial disparities in health care access and delivery, and to skilled esophageal surgeons is warranted to improve survival for all patients, particularly Blacks.
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KEY WORDS: cancer disparity; epidemiology; health care delivery

INTRODUCTION

Esophageal cancer is a highly lethal cancer whose occurrence is more frequent among minorities [1]. Previous epidemiologic studies have consistently reported that blacks in the US have higher incidence and mortality rates than their white counterparts. Blacks experience higher rates of squamous cell cancer (SCC), while white patients present more frequently with adenocarcinoma (AC); exposures to different, specific risk factors have been hypothesized to explain these findings. SCC is typically associated with smoking, drinking, and a diet poor in vitamins and nutrients from fruit and vegetables, something that has been observed more frequently among minorities and patients with low socio-economic status [2]. AC is associated with Barrett's esophagus and acid reflux, a pathology occurring more frequently in whites [3]. The high frequency of SCC, which is associated with worse survival compared to AC, in blacks has been proposed as one of the reasons for the higher mortality observed in this group. However, other factors, such as access to early diagnosis and better quality treatment, are likely to affect survival, and may differ according to race. Several analyses of the Surveillance, Epidemiology, and End Results (SEER) data, a large population-based dataset, or other publicly available data sets, have also shown that black patients with EC experience worse survival than whites, and have suggested that this may be due to the low rate of surgery in blacks [4–9]. In fact, in the study where mortality data were adjusted for having had esophagectomy, outcome disparities were attenuated or eliminated altogether [6]. Such conclusion from this study was, however, limited by the small sample of black patients; other similar studies were hampered by the selection of specific non-generalizable populations such as veterans [7] or the elderly [5].

The present analysis was conducted with the following aims: (i) to study the effect of cancer-directed surgery on mortality in a large population of black and white patients with EC and (ii) to study the determinants of surgery according to race.

MATERIALS AND METHODS

The SEER database was analyzed from 1973 to 2011 to identify all cases of pathologically-proven local and locoregional AC and SCC of the esophagus (tumor site codes 15.1–15.5, 15.8, 15.9; morphology codes 8000–8030, 8033, 8041, 8051, 8070–8075, 8120, 8123, 8140–8145, 8210, 8211, 8260, 8460, 8481, 8560, 8800–01, 8980). The SEER 09 registry includes data from 9 US registries, from 1973–2004; the SEER 17 registry includes cases from 17 registries, from 2000 to 2004; the SEER 18 registry includes cases from greater Georgia from 2000 forward, with the exception of adjustments for the areas impacted by Hurricanes Katrina and Rita.

The following cases were excluded (Fig. 1): patients under age 18 years, diagnosed postmortem, non-microscopically confirmed,

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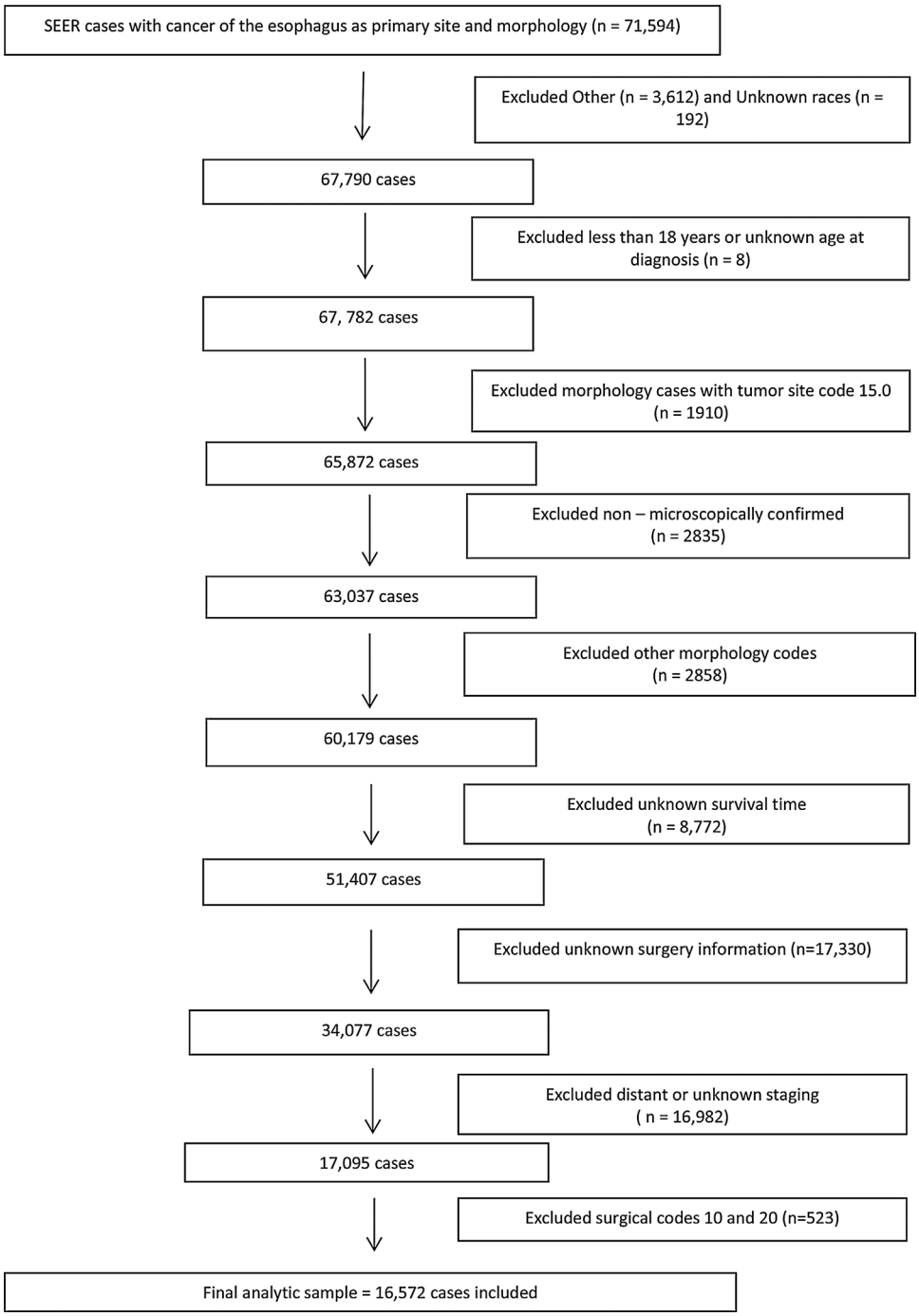

Fig. 1. Flow diagram of exclusion criteria.

patients without survival time recorded in the database, unknown surgical status, histologies other than SCC or AC, and cervical esophageal cancer (tumor site 15.0; n = 1,565 Whites and n = 345 Blacks).

Definition of Staging

To ensure consistent definitions across all years, staging was examined using the SEER historic stage. A variable, which defines "localized" as cancer limited to the primary organ and "regionalized" as cancer extending beyond the primary organ to nearby lymph nodes or tissue. Cases with metastases or no staging were excluded.

Definition of Cancer-Directed Surgery

Patients were categorized as having received cancer-directed surgery if any of the following codes were indicated for the site-specific surgery variable: 30 = partial esophagectomy; 40 = total

esophagectomy; 50, 60, 70 = total or partial esophagectomy, not otherwise specified; 80 = esophagectomy, not otherwise specified. Patients with codes 10 = local tumor destruction, not otherwise specified, and 20 = local tumor excision, not otherwise specified (n = 523) were excluded.

Patients who did not undergo cancer-directed surgery were those associated with the code 00 (which indicated "no surgical procedure had been performed") and codes for other types of surgery that are not cancer-directed, including incisional biopsies, exploratory-only surgery, palliative bypasses, and non-cancer directed surgery (01, 02, 03, 04, 05, 06, 07).

Definition of Radiation Therapy

For all cases, the "RX summary radiation" variable was used to examine whether patients had received radiation therapy. Patients were categorized as having received radiation therapy if the following categories were indicated: (1 = beam radiation, 2 = radioactive implants, 3 = radioisotopes, 4 = combination of beam with implants or isotopes, 5 = radiation (method or source not otherwise specified), or other radiation (cases from 1973–1987 only). Patients were categorized as having not received radiation if the categories "0 = none" or "7 = patient or patient's guardian refused" were indicated. The categories "8 = recommended, unknown if administered" and "9 = unknown if radiation administered" were combined to categorize patients as unknown radiation status.

Statistical Analysis

Age, sex, diagnosis year, stage, cancer-directed surgery, radiation, and vital status were analyzed (chemotherapy data not available) according to self-reported race (Black and White). Comparisons between black and white patients were performed using the *t*-test for continuous variables and chi-square test for categorical variables. Overall survival was defined as the time between initial date of diagnosis and the date of death or censored at date of last follow-up. Comparison of survival between blacks and whites was performed using multivariable regression based on a Cox proportional hazards model. The independent association between race, age, histology and stage, and whether a patient underwent cancer-directed surgery was analyzed using a logistic regression model, in which cancer-directed surgery (yes/no) was the dependent variable. All analyses were performed using Stata/SE version 12 (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP).

RESULTS

Among the 13,678 white and 2,894 black patients with EC extracted from the SEER data base, the incidence was 1.9 per 100,000 Whites and 3.9 per 100,000 Blacks (age adjusted, $P = <0.0001$). Among white patients, the incidence of SCC remained low and constant over the years, while the incidence of AC began increasing in the early 1980s, leveling off in the 2000s (Fig. 2). Among blacks, the number of new AC cases was low and constant over the years, while the incidence of SCC began decreasing in the early 1990s (Fig. 2). Black patients with EC were diagnosed at a significantly younger age (62 vs. 68 years; $P < 0.0001$), and with a significantly higher proportion of SCC (96% vs. 50%; $P < 0.0001$) compared to white patients (Table I).

The frequency of cancer-directed surgery was significantly lower among blacks than whites (40% vs. 53%; $P < 0.0001$), while the frequency of radiation was higher in black compared to white patients, but unlikely to be clinically significant (65% vs. 62%; $P < 0.0001$). When the combination of surgery and radiation was analyzed, a higher proportion of Blacks compared to Whites did not undergo either treatment or were treated with radiation and no surgery (Table I). The difference in patients undergoing either treatment (14% vs. 12%) is not clinically significant. Overall survival was significantly lower in black than in white patients (20.3 vs. 28 months; $P < 0.0001$; Fig. 2). Survival improved over the years in both ethnic groups (Table II).

On multivariable analysis, predictors associated with higher mortality at 1 year were: black race, HR_{adj}: 1.24 (95% CI: 1.16–1.32); older age, HR_{adj} 1.02 (95% CI: 1.01–1.02) for every year increase in age; advanced stage, HR_{adj} 1.6 (95% CI: 1.53–1.69) for regional versus localized EC; and SCC histology, HR_{adj} 1.22 (95% CI: 1.55–1.30) versus AC. Treatment, either surgery alone or in combination with radiotherapy, significantly improved survival compared to not undergoing surgery or radiation (Table II). When the analysis was stratified by histologic type (Table II), black race was an independent predictor of higher mortality in SCC cases only, HR_{adj} 1.21 (95% CI: 1.13–1.30). Although regional (compared to localized) stage was associated with higher mortality in both histologic types, the effect was stronger in AC, HR_{adj} 1.78 (95% CI: 1.63–1.94) in AC and HR_{adj} 1.48 (95% CI: 1.39–1.58) in SCC.

White patients demonstrated better survival for localized EC (Fig. 3a). If cancer-directed surgery was performed, black patients experienced significantly lower survival than their white counterparts (Fig. 3b). The effect of race was not significant for patients who did not undergo cancer-directed surgery (Fig. 3c) or radiation. These differences were seen among regional cases as well (data not shown).

The factors associated with undergoing cancer-directed surgery were analyzed in a multivariable model (Table III): Blacks were significantly less likely to undergo surgery than Whites, OR_{adj}: 0.59 (95% CI: 0.54–0.65). Patients with regional EC were less likely to undergo cancer-directed surgery than those with localized EC, OR_{adj}: 0.74 (95% CI: 0.69–0.79). Patients with SCC were significantly less likely to undergo cancer-directed surgery compared to those with AC, OR_{adj}: 0.43 (95% CI: 0.40–0.46).

DISCUSSION

This updated analysis of the large SEER population of white and black patients with EC supports others' findings with regard to histology, race, and outcome. First, the incidence of SCC in blacks continues to be significantly higher than in whites in agreement with what other authors have reported in the past [10]. The finding of a decrease in the incidence of SCC and increase in that of AC over the decades also confirms previously reported conclusions. The rise of obesity [3] and gastroesophageal reflux [11] has likely contributed to the increasing incidence of AC over the years. The observation of a decrease in the incidence of SCC among blacks may reflect reductions in the rates of smoking and alcohol consumption in this population [2].

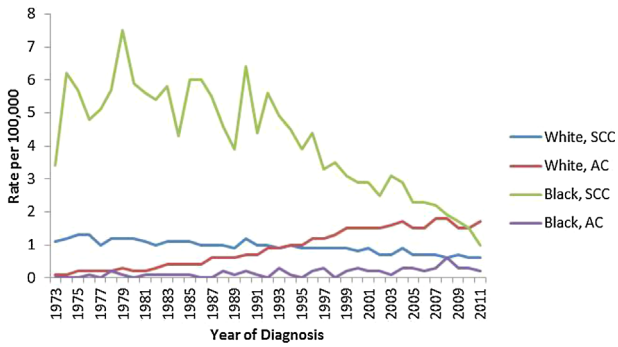

Fig. 2. Esophageal cancer incidence by race and histology; SCC, squamous cell carcinoma; AC, adenocarcinoma.

TABLE I. Characteristics of Esophageal Cancer Cases According to Race (n = 16,572)

Variable	Categories	Whites (n = 13,678)	Blacks (n = 2,894)	*P*-value
Sex	Male	10,168 (74%)	2,079 (72%)	0.005
	Female	3,510 (26%)	815 (28%)	
Mean age in year (95% CI)		67.8 (10.7)	61.6 (10.5)	<0.0001
Overall stage	Localized	6,609 (48%)	1,508 (52%)	<0.0001
	Regional	7,069 (52%)	1,386 (48%)	
Histology	SCC	6,775 (50%)	2,777 (96%)	<0.0001
	Adenocarcinoma	6,903 (50%)	117 (4%)	
Cancer-directed surgery	No	6,428 (47%)	1,726 (60%)	<0.0001
	Yes	7,250 (53%)	1,168 (40%)	
Radiation	No	4,960 (36%)	935 (32%)	<0.0001
	Yes	8,476 (62%)	1,870 (65%)	
	Unknown	242 (2%)	89 (3%)	
Therapy	None	1,619 (12%)	411 (14%)	<0.0001
	Surgery only	3,341 (25%)	524 (19%)	
	Radiation only	4,678 (35%)	1,258 (45%)	
	Both surgery and radiation overall	3,798 (28%)	612 (22%)	
Mean survival in months (95% CI)		28.2 (4.4)	20.3 (3.7)	<0.0001
	1973–1990	25.5 (5.5)	18.3 (3.9)	
	1991–2000	35.2 (5.7)	25.2 (4.2)	
	2001–2010	24.9 (2.8)	19.1 (2.3)	

SEER, surveillance, epidemiology, and end results.

Independent of the influence of stage, black, and white EC patients experienced similar survival when no cancer-directed surgery was performed. If they underwent cancer-directed surgery, black EC patients experienced significantly lower survival than white EC patients. Although the reasons for this disparity are not clear, one hypothesis is that EC health care delivery may differ with race: blacks may not be staged adequately, may undergo esophagectomy at less experienced and/or low volume centers, or may not receive appropriate induction and/or adjuvant therapy. It is also possible that black patients lack access to more experienced, specialized thoracic surgeons who perform oncologic resections. Several studies have demonstrated racial disparities in referral to high-volume hospitals, which may represent a proxy for better quality care [12,13]. As information regarding hospital volume or specialty of the surgeon performing esophagectomy is not available in the SEER database, the present analysis cannot evaluate these hypotheses.

Among treatment options available for EC, the SEER database reports information regarding cancer-directed surgery and radiation, and not chemotherapy. In this context, the current analysis confirms that black EC patients receive less cancer-directed surgery, but more radiotherapy than whites. A lower rate of cancer-directed surgery in black EC patients has been previously described in other SEER dataset analyses on a smaller sample size [5,6]. The reason for a lower rate of cancer-directed surgery among blacks may be that fewer Blacks are offered this treatment option, or that more Blacks decline surgery and/or have comorbidities that contraindicate esophagectomy. A previous study [4] reported that black EC patients were less likely to be seen by a surgeon, and if seen, they were less likely to be offered surgery. Given limitations of available information and retrospective nature of the current study, further conclusions regarding these issues cannot be made. We can conclude, however, that black race was independently associated with not undergoing cancer-directed surgery, regardless of age, gender, stage, and histology.

TABLE II. Determinants of 1-Year Mortality in EC Patients, Overall and by Histologic Type

	Overall	SCC	AC
Variable		Adjusted HR (95% CI)*	
Race			
Black versus white	1.24 (1.16–1.32)	1.21 (1.13–1.30)	1.06 (0.77–1.45)
Sex			
Female versus male	0.95 (0.90–1.01)	0.94 (0.88–1.00)	0.97 (0.86–1.09)
Age			
Per increased year	1.02 (1.01–1.02)	1.01 (1.01–1.02)	1.02 (1.02–1.02)
Stage			
Regional versus localized	1.60 (1.53–1.69)	1.48 (1.39–1.58)	1.78 (1.63–1.94)
Histology			
SCC versus AC	1.22 (1.15–1.30)	–	–
Therapy			
None	1.0 (REF)	1.0 (REF)	1.0 (REF)
Surgery only	0.30 (0.27–0.33)	0.31 (0.28–0.35)	0.27 (0.24–0.31)
Radiation only	0.56 (0.52–0.60)	0.53 (0.48–0.58)	0.63 (0.56–0.72)
Both surgery and radiation	0.34 (0.31–0.37)	0.36 (0.32–0.40)	0.30 (0.26–0.35)
Year of diagnosis			
Per increased year	0.97 (0.97–0.97)	0.97 (0.97–0.98)	0.96 (0.96–0.97)

SCC, squamous cell carcinoma; AC, adenocarcinoma.
*Adjusted for all other variables in the table.

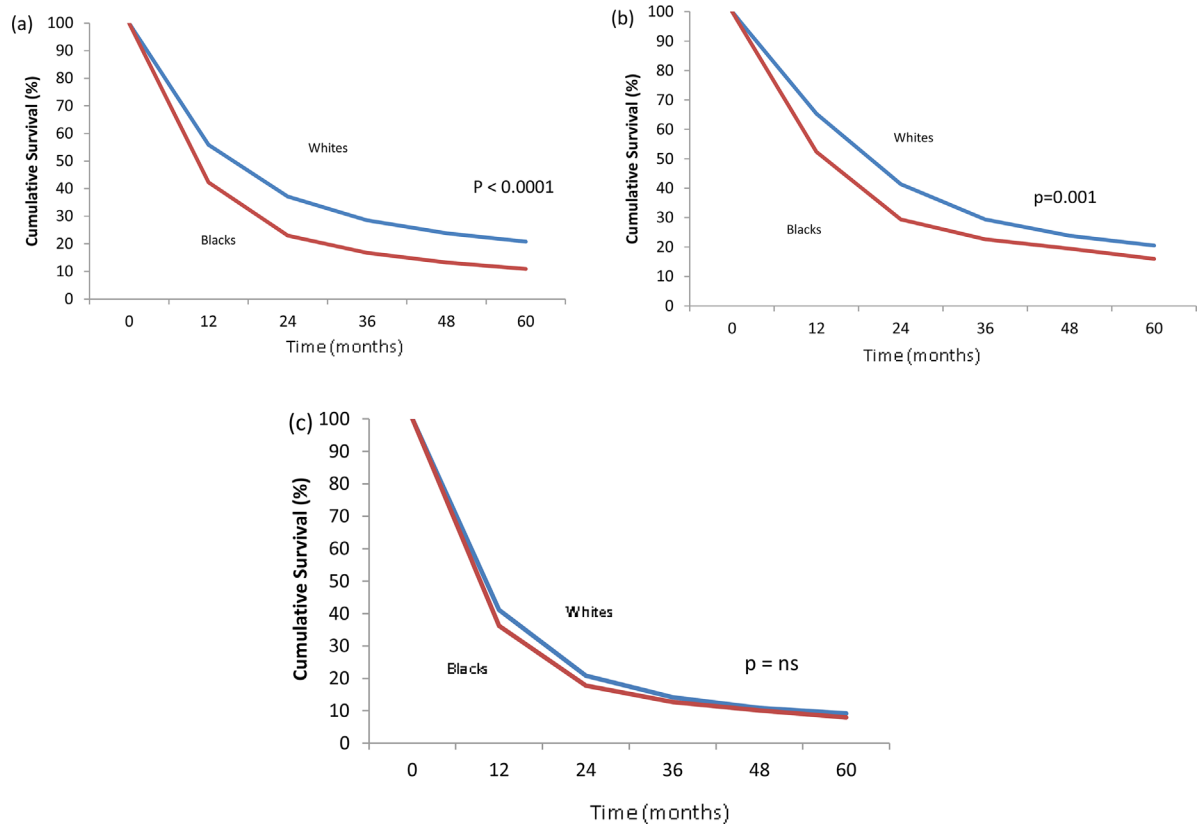

Fig. 3. Survival in localized EC.

We report here that overall survival for EC in blacks is significantly lower than in whites, even when presenting at similar stage. Our data suggest that difference in care delivery patterns, in particular, rates of cancer-directed surgery, between the races may contribute to racial disparities in mortality and survival. Others reported that once adjusting for esophagectomy, there was no longer racial disparity in EC survival [6]. Although we confirmed that black EC patients underwent significantly less cancer-directed surgery than whites, we found that differences in survival persisted, even when adjusted for cancer-directed surgery. Our analysis suggests that black race is a more important risk factor than previously thought, either per se or as a proxy of other factors that differentially affect black patients. While stage at diagnosis was similar for black and white patients in the SEER dataset, and the analysis was adjusted for stage regardless, it is possible that black patients are more likely to suffer stage-independent biologically more aggressive tumors. Additional factors, such as preoperative and postoperative care, induction and/or adjuvant therapy, and possible disparities in access or willingness to receive chemotherapy may be involved.

Although cancer-directed surgery was associated with lower EC mortality, the 1-year mortality for blacks who underwent cancer-directed surgery in the SEER dataset was significantly higher than for their white counterparts. This findings suggests that the surgery black patients receive is associated with increased mortality. Investigation into racial disparities in quality of health care access and delivery, including skilled esophageal surgeons is warranted to improve survival in black patients with EC.

TABLE III. Predictors of Whether EC Is Treated With Surgery

Variable	OR_{adj} (95% CI)*
Race	
Black versus white	0.59 (0.54–0.65)
Sex	
Female versus male	1.06 (0.98–1.15)
Age	
Per year increase	0.96 (0.95–0.96)
Stage	
Regional versus localized	0.74 (0.69–0.79)
Histology	
SCC versus AC	0.43 (0.40–0.46)
Year of diagnosis	
Per year	0.98 (0.97–0.99)

*Adjusted for all other variables in the table.

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