Original Article

Treatment disparities affect outcomes for patients with stage I esophageal cancer: a national cancer data base analysis

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Background: To examine patterns of care and outcomes for patients with stage I esophageal cancer (EC) in the United States.

Methods: We identified patients in the National Cancer Data Base diagnosed with stage I EC from 2004 to 2012 and grouped them by primary treatment: esophagectomy (Eso), local excision (LE), concurrent chemoradiation (CRT), or observation (Obs). Multinomial logistic regression was used to predict receipt of treatments. Overall survival (OS) was estimated by Kaplan-Meier methods adjusted for inverse probability of treatment weighting (IPTW) and Cox proportional hazard regressions.

Results: Of 5,480 patients, 2,312 (42%) underwent Eso, 1,250 (23%) LE, 758 (14%) CRT, and 1,160 (21%) Obs. LE use increased over time from 17% to 29% while Obs declined from 26% to 19%. Patients least likely to undergo surgery were older, had greater comorbidity, were uninsured, were treated at non-academic centers, and were Black. The rate of surgery for Black patients was half of that for White patients (33% *vs.* 67%). Postoperative mortality rates were higher after Eso *vs.* LE at 30 days (2.9% *vs.* 0.5%; P<0.001) and at 90 days (5.5% *vs.* 1.4%, P<0.001). Five-year OS was 59% with Eso, 63% LE, 29% CRT, and 31% Obs (P<0.001). On multivariate analysis, outcomes were best after LE [*vs.* Eso: hazard ratio (HR) =1.15, 95% CI: 1.01–1.30, P=0.037; CRT: HR =2.41, 95% CI: 2.09–2.78, P<0.001; Obs: HR =3.79, 95% CI: 3.33–4.32, P<0.001).

Conclusions: Disparities are evident in the care of patients with stage I EC throughout the United States. LE was associated with favorable outcomes compared to Eso, CRT, and Obs.

Keywords: Stage I esophageal cancer; esophagectomy; chemoradiation (CRT); disparities

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Introduction

The incidence of esophageal cancer (EC) continues to rise in the Western world because of several prevalent risk factors including obesity, tobacco smoking, and Barrett's esophagus (1). Although overall long-term prognosis is poor at 18%, high cure rates can be achieved when the disease is diagnosed early (2). Historically, esophagectomy (Eso) was considered the classic treatment for stage I EC. However, advancements in endoscopic therapies including ablation and local excision (LE) have resulted in comparable to superior EC-related mortality and overall survival (OS), making LE an acceptable alternative to esophagectomy (Eso)for select clinical T1 EC (3,4). For patients who cannot or choose not to undergo surgery, definitive chemoradiation (CRT) is the recommended treatment (5).

Despite these national guidelines, sociodemographic disparities influencing treatment selection are an unfortunate

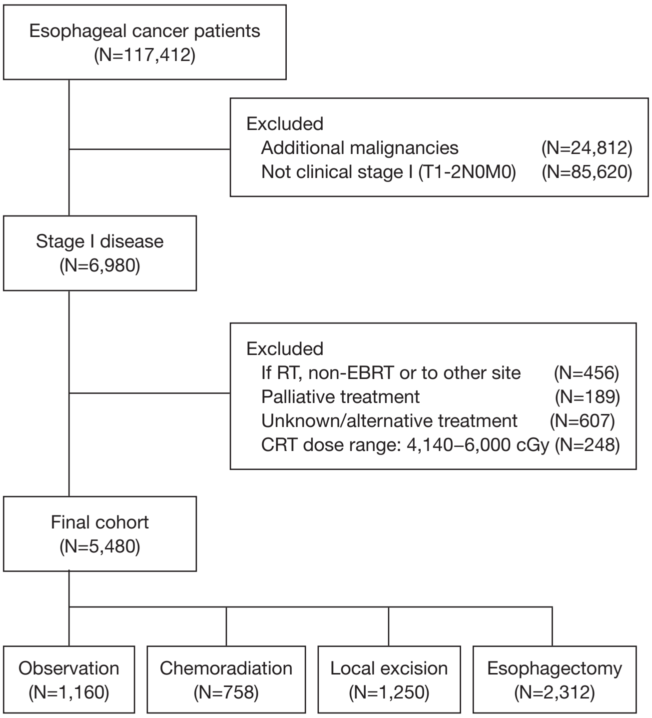

Figure 1 Flow diagram. CRT, chemoradiation; EBRT, external beam radiation therapy.

reality and pose challenges at all levels of cancer-directed treatment. From potential underutilization of cancer screening among ethnic minorities to the underutilization of surgical management for elderly patients with EC, cancer outcomes can be negatively affected in subsets of patients because of ongoing discrepancies in healthcare (6-9).

In the current literature on stage I EC, most observational studies provide comparisons between surgical methods or highlight treatment disparities among elderly patients, with most studies being restricted to Medicare-eligible patients (10-13). Information is limited on comprehensive treatment patterns and outcomes for all patients with stage I EC, particularly in the modern era. By using the National Cancer Data Base (NCDB), an extensive dataset that captures more than 70% of all newly diagnosed cancer cases nationwide (14), we examined the use of Eso, LE, CRT, and observation (Obs) for stage I EC, with a particular focus on disparities in treatment selection and the potential effect of such disparities on survival.

Methods

The NCDB is a nationwide clinical surveillance resource originally established in 1989 by the American Cancer Society and the Commission on Cancer (CoC) of the American College of Surgeons. De-identified oncologic data are acquired annually from more than 1,500 CoC-approved centers and are standardized by rules similar to those used for the Surveillance, Epidemiology, and End Results (SEER) registry. Data include patient demographics, socioeconomic status, tumor characteristics, initial course of therapy, and OS in addition to radiation therapy specifics, making the NCDB a valuable investigative tool (15). This study was exempt from Institutional Review Board evaluation as the information utilized was de-identified.

We first identified 6,980 patients as having been diagnosed with clinical T1–2N0 EC in 2004–2012; 5,480 were included in this study (*Figure 1*). Patients with cT2 disease were included only if they had been diagnosed in 2010–2012 to reflect the implementation of the 7th American Joint Commission on Cancer staging system. Patients were grouped according to treatment: Eso, LE, CRT, or Obs. CRT consisted of concurrent CRT (radiation dose range, 41.4–60 Gy) with chemotherapy begun within 14 days of starting radiation therapy. Those in the Obs group did not receive any form of therapy.

Type of treatment facility was dichotomized into academic/research (AR) or non-academic (non-AR) facilities, the latter consisting of community cancer programs or comprehensive community cancer programs. Hospital volume for a given surgery was defined as the mean annual caseload, which was calculated by dividing the total number of surgical procedures performed at a given institution by the number of years in the study period. Hospital volume was then stratified into quintiles, with the highest 20% considered "high volume" facilities, the middle 60% "medium volume", and the remaining 20% "low volume". Distance from treating facility was categorized as either local (0–25 miles) or distant (>25 miles).

Baseline patient sociodemographic, clinical, and facility characteristics were compared among the treatment groups with Pearson χ^2 tests. Multinomial logistic regression was used to examine correlations between covariates and treatment selection. Covariates in the model included year of diagnosis, age group, sex, race, comorbidity score, income quartiles, type of insurance, tumor location, facility type, and distance from facility. Thirty- and 90-day postoperative mortality rates (among surgical patients), 5-year OS estimates, and hazard ratios (HR) were analyzed. To reduce selection bias, outcomes other than postoperative mortality were adjusted by using the inverse probability of treatment weighting (IPTW) method. To obtain the IPTW reflecting the differences in sample sizes for the three treatment groups, a generalized logit function was used to contrast a reference group to the other three groups, in which propensity scores to conditionally predict a patient's probability of receiving a particular treatment were obtained after adjustment for the covariates. The IPTW method, which is based on propensity scores, calculates a weight for each subject that equals the inverse of the probability of receiving the treatment actually received (16-18). These weights, in turn, are incorporated into the survival analysis to enhance the robustness of the analysis. The IPTW-adjusted patient, tumor, and treatment characteristics are shown in *Table S1*. Statistical analyses were done with SAS v9.4 (Cary, NC, USA).

Results

Patients

Baseline characteristics of all patients are shown in *Table 1*. Of 5,480 patients, 2,312 (42%) were treated with Eso, 1,250 (23%) LE, 758 (14%) CRT, and 1,160 (21%) Obs. Over time, the use of LE increased from 17% to 29%, while use of Obs declined from 26% to 19% (*Figure 2*). Surgical management was more often performed in ARs (n=2,321, 65% of all surgeries) than in non-ARs (n=1,241, 35%). Median age at diagnosis was 67 years (range, 19–90 years) for the entire group and was highest in the Obs group at 73 years (range, 34–90 years). A treatment-selection pattern by age was evident. Specifically, the proportion of patients undergoing LE, CRT, and Obs increased with age, whereas use of Eso decreased with age. A higher proportion of men than women received Eso (44% *vs.* 34%) or LE (23% *vs.* 20%). However, age was again a likely driving factor, because twice as many women were ≥80 years old at diagnosis (24%) as were men (11%). Additional pertinent characteristics included 71% of patients having a comorbidity score of 0 and 69% having a tumor in the lower third of the esophagus.

Analysis by race revealed that 308 patients (5.6%) were Black and 4,971 (90.7%) were White. On average, Blacks were younger at diagnosis than Whites [age 63 years (range, 28–90 years) *vs.* 68 years (range, 19–90 years)]. The rate of any surgery for Black patients was half that for White patients (33% *vs.* 67%), and the rate of Obs was disproportionately higher among Black patients (38% *vs.* 20%). Differences in treatment selection may have been influenced by the greater proportion of Blacks having comorbidity scores ≥2 (11% *vs.* 7% of Whites). However, other socioeconomic factors such as type of insurance and median household income may have influenced the observed discrepancies. Compared with Whites, Blacks were more often uninsured (5.8% *vs.* 1.6%) or on Medicaid (19% *vs.* 3.5%), and belonged to lower median income quartiles (<$30,000: 36% Blacks *vs.* 10% Whites). Yet even within the highest income quartile (≥$46,000), the rate of nonsurgical management was disproportionately higher among Blacks *vs.* Whites: CRT, 27% *vs.* 11%; and Obs, 33% *vs.* 20% (*Table S2*).

Factors affecting treatment selection

Racial disparities were again evident in our multinomial logistic regression model, as Blacks were less likely to undergo LE [odds ratio (OR) =0.25, 95% confidence interval (CI): 0.15–0.42, P<0.001] or Eso (OR =0.43, 95% CI: 0.31–0.61, P<0.001) than White patients (*Table 2*). Patients belonging to the lowest median income quartile were less likely to undergo LE (OR =0.36, 95% CI: 0.26–0.51, P<0.001) or Eso (OR =0.52, 95% CI: 0.39–0.69, P<0.001) than patients in the top income quartile. Reduced odds of having surgery were also seen for uninsured patients and treatment at non-ARs compared with ARs (LE OR =0.21, 95% CI: 0.18–0.26, P<0.001; Eso OR =0.37, 95% CI: 0.31–0.44, P<0.001). Other noteworthy factors that reduced the probability of undergoing Eso or LE included having a comorbidity score of ≥2, a tumor located outside the lower third of the esophagus, and living 0–25 miles from the treating facility. Only the odds of undergoing LE were significantly influenced by year of diagnosis, with an interval increase in those odds with each year after 2007.

Outcomes

Among the facilities performing surgical procedures, the mean annual hospital volume was 22 Eso cases and 34 LE cases (range, 1–159 cases). Overall 30-day postoperative mortality rates were 3.1% at low-volume facilities, 2.1% at medium-volume facilities, and 1% at high-volume facilities (P=0.022), and corresponding 90-day postoperative mortality rates were 6.7%, 3.7%, and 2.1% (P<0.001). When stratified by type of procedure, postoperative mortality was worse after Eso than after LE, both at 30 days (2.9% *vs.* 0.5%, P<0.001) and at 90 days (5.5% *vs.* 1.4%, P<0.001).

To best mimic a well-balanced cohort, we adjusted the

Table 1 Baseline patient and treatment characteristics

Characteristic	All (n=5,480)	Observation (n=1,160)	Treatment group			P value
			CRT (n=758)	LE (n=1,250)	Eso (n=2,312)	
Age at diagnosis, years	67 [19–90]	73 [34–90]	71 [19–90]	69 [29–90]	63 [24–90]	
Age group, n (%)						<0.001
≤50 years	394 (7.2)	56 (4.8)	29 (3.8)	67 (5.4)	242 (10.5)	
51–60 years	1,153 (21.1)	170 (14.7)	129 (17.0)	220 (17.6)	634 (27.4)	
61–70 years	1,745 (31.8)	280 (24.1)	213 (28.1)	397 (31.8)	855 (37)	
71–80 years	1,443 (26.3)	300 (25.9)	257 (33.9)	375 (30.0)	511 (22.1)	
>80 years	745 (13.6)	354 (30.5)	130 (17.2)	191 (15.3)	70 (3.0)	
Sex, n (%)						<0.001
Male	4,352 (79.4)	846 (72.9)	563 (74.3)	1,020 (81.6)	1,923 (83.2)	
Female	1,128 (20.6)	314 (27.1)	195 (25.7)	230 (18.4)	389 (16.8)	
Race, n (%)						<0.001
White	4,971 (90.7)	997 (85.9)	646 (85.2)	1,166 (93.3)	2,162 (93.5)	
Black	308 (5.6)	116 (10.0)	89 (11.7)	21 (1.7)	82 (3.6)	
Other	201 (3.7)	47 (4.1)	23 (3.0)	63 (5.0)	68 (2.9)	
Comorbidity score, n (%)						<0.001
0	3,907 (71.3)	785 (67.7)	528 (69.7)	952 (76.2)	1,642 (71.0)	
1	1,154 (21.1)	245 (21.1)	165 (21.8)	210 (16.8)	534 (23.1)	
≥2	419 (7.6)	130 (11.2)	65 (8.5)	88 (7.0)	136 (5.9)	
Median household income, n (%)						<0.001
<$30,000	608 (11.1)	152 (13.1)	140 (18.5)	92 (7.4)	224 (9.7)	
$30,000–$34,999	973 (17.8)	205 (17.7)	136 (17.9)	219 (17.5)	413 (17.9)	
$35,000–$45,000	1,564 (28.5)	317 (27.3)	208 (27.4)	364 (29.1)	675 (29.2)	
≥$46,000	2,101 (38.3)	432 (37.2)	232 (30.6)	525 (42.0)	913 (39.5)	
Unknown	233 (4.3)	54 (4.7)	42 (5.5)	50 (4.0)	87 (3.8)	
Medical insurance, n (%)						<0.001
Uninsured	103 (1.9)	38 (3.3)	18 (2.4)	10 (0.8)	37 (1.6)	
Private	1,917 (35.0)	283 (24.4)	179 (23.6)	405 (32.4)	1,050 (45.4)	
Medicaid	245 (4.5)	47 (4.1)	52 (6.9)	39 (3.1)	107 (4.6)	
Medicare	3,029 (55.3)	753 (64.9)	483 (63.7)	741 (59.3)	1,052 (45.5)	
Other government	91 (1.7)	16 (1.4)	15 (2.0)	25 (2.0)	35 (1.5)	
Unknown	95 (1.7)	23 (2)	11 (1.5)	30 (2.4)	31 (1.3)	

Table 1 *(continued)*

Table 1 *(continued)*

Characteristic	All (n=5,480)	Observation (n=1,160)	Treatment group			P value
			CRT (n=758)	LE (n=1,250)	Eso (n=2,312)	
Community type, n (%)						0.117
Metro	4,327 (79.0)	941 (81.1)	587 (77.4)	1,004 (80.3)	1,795 (77.6)	
Urban	819 (14.9)	148 (12.8)	123 (16.2)	174 (13.9)	374 (16.2)	
Rural	113 (2.1)	19 (1.6)	21 (2.8)	22 (1.8)	51 (2.2)	
Unknown	221 (4.0)	52 (4.5)	27 (3.6)	50 (4.0)	92 (4.0)	
Esophageal tumor location, n (%)						<0.001
Lower third	3,756 (68.5)	626 (54.0)	473 (62.4)	876 (70.1)	1,781 (77.0)	
Middle third	723 (13.2)	194 (16.7)	123 (16.2)	170 (13.6)	236 (10.2)	
Upper third	210 (3.8)	63 (5.4)	75 (9.9)	37 (3.0)	35 (1.5)	
Unknown	791 (14.4)	277 (23.9)	87 (11.5)	167 (13.4)	260 (11.3)	
Tumor histology, n (%)						<0.001
Adenocarcinoma	4,132 (75.4)	742 (64.0)	470 (62.0)	1,028 (82.2)	1,892 (81.8)	
Squamous cell carcinoma	895 (16.3)	299 (25.8)	254 (33.5)	82 (6.6)	260 (11.2)	
Other/unknown	453 (8.3)	119 (10.3)	34 (4.5)	140 (11.2)	160 (6.9)	
Facility type, n (%)						<0.001
Academic	2,901 (52.9)	349 (30.1)	231 (30.5)	926 (74.1)	1,395 (60.3)	
Non-academic	2,579 (47.1)	811 (69.9)	527 (69.5)	324 (25.9)	917 (39.7)	
Distance from facility, n (%)						<0.001
0–25 miles	3,401 (62.1)	942 (81.2)	595 (78.5)	574 (45.9)	1,290 (55.8)	
>25 miles	2,079 (37.9)	218 (18.8)	163 (21.5)	676 (54.1)	1,022 (44.2)	
Year of diagnosis, n (%)						<0.001
2004	333 (6.1)	85 (7.3)	60 (7.9)	56 (4.5)	132 (5.7)	
2005	354 (6.5)	87 (7.5)	53 (7.0)	60 (4.8)	154 (6.7)	
2006	381 (7.0)	113 (9.7)	50 (6.6)	51 (4.1)	167 (7.2)	
2007	474 (8.7)	104 (9.0)	68 (9.0)	88 (7.0)	214 (9.3)	
2008	651 (11.9)	150 (12.9)	72 (9.5)	148 (11.8)	281 (12.2)	
2009	753 (13.7)	160 (13.8)	88 (11.6)	174 (13.9)	331 (14.3)	
2010	861 (15.7)	163 (14.1)	120 (15.8)	216 (17.3)	362 (15.7)	
2011	812 (14.8)	138 (11.9)	116 (15.3)	209 (16.7)	349 (15.1)	
2012	861 (15.7)	160 (13.8)	131 (17.3)	248 (19.8)	322 (13.9)	

CRT, concurrent chemoradiation; LE, local excision; Eso, esophagectomy.

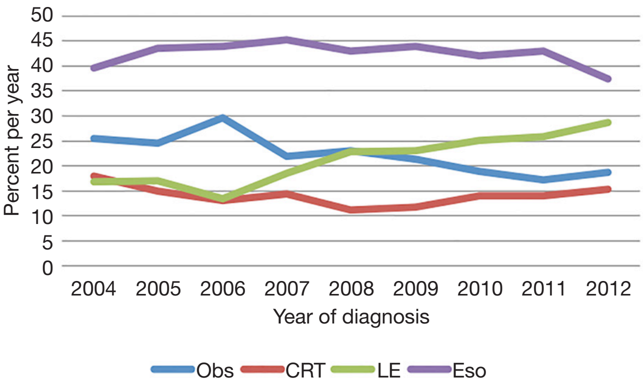

Figure 2 Temporal trends in treatment selection for stage I esophageal cancer from 2004 through 2012. CRT, chemoradiation; Eso, esophagectomy; LE, local excision; Obs, observation.

treatment groups by using propensity score-weighted measurements (IPTW) to obtain balanced comparison groups, in which no significant differences were found in any of the covariates to be modeled in the analysis (*Table S1*). Median survival times, in months, by treatment group were: 90 for Eso, 116 for LE, 29 for CRT, and 22 for Obs. The IPTW-adjusted Kaplan-Meier curves are shown in *Figure 3*, with the highest 5-year OS estimates belonging to the LE group at 63% followed by 59% for Eso, 31% for Obs, and 29% for CRT (P<0.001).

In our IPTW-adjusted Cox modeling analysis (*Table 3*), all treatments were associated with worse outcomes relative to LE: Eso HR =1.15, 95% CI: 1.01–1.30, P=0.037; CRT HR =2.41, 95% CI: 2.09–2.78, P<0.001; and Obs

Table 2 Odds ratios of undergoing a select treatment by multinomial logistic regression models

Variable	Treatment group					
	CRT		LE		Eso	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age group, years						
≤50	1		1		1	
51–60	1.56 (0.93–2.61)	0.09	0.83 (0.54–1.3)	0.415	0.69 (0.48–1.0)	0.05
61–70	1.56 (0.94–2.59)	0.089	0.79 (0.51–1.22)	0.285	0.54 (0.38–0.78)	<0.001
71–80	1.81 (1.08–3.05)	0.026	0.79 (0.51–1.24)	0.312	0.34 (0.23–0.5)	<0.001
>80	0.77 (0.45–1.32)	0.335	0.37 (0.23–0.59)	<0.001	0.04 (0.03–0.06)	<0.001
Sex						
Male	1		1		1	
Female	1.01 (0.81–1.27)	0.901	0.79 (0.64–0.99)	0.038	0.87 (0.71–1.06)	0.155
Race						
White	1		1		1	
Black	0.99 (0.71–1.37)	0.931	0.25 (0.15–0.42)	<0.001	0.43 (0.31–0.61)	<0.001
Other	0.78 (0.46–1.33)	0.363	0.91 (0.59–1.4)	0.664	0.56 (0.36–0.86)	0.008
Comorbidity score						
0	1		1		1	
1	0.96 (0.76–1.21)	0.717	0.81 (0.65–1.02)	0.073	1.23 (1.01–1.5)	0.044
≥2	0.65 (0.47–0.91)	0.011	0.58 (0.42–0.8)	0.001	0.54 (0.41–0.72)	<0.001

Table 2 *(continued)*

Table 2 *(continued)*

Variable	Treatment group					
	CRT		LE		Eso	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Year of diagnosis						
2004	1		1		1	
2005	0.84 (0.51–1.36)	0.469	1.04 (0.62–1.75)	0.872	1.19 (0.77–1.82)	0.437
2006	0.66 (0.41–1.07)	0.093	0.60 (0.36–1.0)	0.052	0.84 (0.55–1.28)	0.415
2007	0.96 (0.61–1.53)	0.877	1.30 (0.80–2.10)	0.296	1.37 (0.91–2.07)	0.129
2008	0.66 (0.42–1.02)	0.063	1.72 (1.10–2.7)	0.018	1.24 (0.85–1.83)	0.265
2009	0.79 (0.51–1.22)	0.283	1.69 (1.09–2.63)	0.02	1.20 (0.82–1.75)	0.348
2010	1.03 (0.68–1.56)	0.9	2.10 (1.36–3.25)	0.001	1.38 (0.95–2.01)	0.089
2011	1.24 (0.81–1.89)	0.324	2.37 (1.52–3.69)	<0.001	1.55 (1.06–2.28)	0.024
2012	1.14 (0.75–1.73)	0.533	2.64 (1.71–4.07)	<0.001	1.22 (0.84–1.78)	0.295
Median income						
≥$46,000 (top quartile)	1		1		1	
$35,000–$45,000	1.17 (0.92–1.50)	0.204	0.78 (0.62–0.97)	0.027	0.88 (0.72–1.08)	0.22
$30,000- $34,999	1.23 (0.93–1.64)	0.153	0.67 (0.52–0.88)	0.004	0.77 (0.61–0.98)	0.033
<$30,000	1.61 (1.18–2.19)	0.003	0.36 (0.26–0.51)	<0.001	0.52 (0.39–0.69)	<0.001
Unknown	1.54 (0.99–2.4)	0.058	0.83 (0.53–1.18)	0.413	0.79 (0.53–1.18)	0.246
Medical insurance						
Medicare	1		1		1	
Private	0.91 (0.7–1.18)	0.463	1.02 (0.80–1.29)	0.891	1.25 (1.01–1.54)	0.037
Medicaid	1.51 (0.95–2.39)	0.084	1.01 (0.61–1.67)	0.969	1.10 (0.73–1.67)	0.644
Other government	1.19 (0.57–2.49)	0.638	1.00 (0.50–2.02)	0.99	0.76 (0.40–1.46)	0.415
Uninsured	0.65 (0.35–1.18)	0.157	0.30 (0.14–0.65)	0.002	0.50 (0.30–0.85)	0.01
Unknown	0.85 (0.40–1.81)	0.676	1.04 (0.56–1.96)	0.893	0.68 (0.37–1.24)	0.207
Esophageal tumor location						
Lower third	1		1		1	
Middle third	0.80 (0.61–1.05)	0.104	0.74 (0.57–0.96)	0.023	0.52 (0.41–0.66)	<0.001
Upper third	1.56 (1.08–2.26)	0.018	0.59 (0.37–0.94)	0.026	0.26 (0.16–0.41)	<0.001
Unknown	0.42 (0.32–0.55)	<0.001	0.50 (0.39–0.64)	<0.001	0.37 (0.30–0.46)	<0.001
Facility type						
Academic	1		1		1	
Non-academic	1.00 (0.81–1.23)	0.969	0.21 (0.18–0.26)	<0.001	0.37 (0.31–0.44)	<0.001
Distance from facility						
0–25 miles	1		1		1	
>25 miles	1.02 (0.80–1.32)	0.852	3.20 (2.58–3.97)	<0.001	2.34 (1.91–2.86)	<0.001

CRT, concurrent chemoradiation; LE, local excision; Eso, esophagectomy; OR, odds ratio; CI, confidence interval.

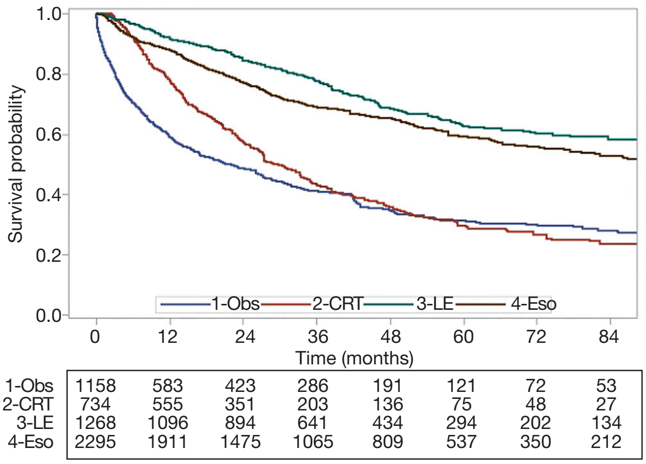

Figure 3 Inverse probability of treatment weighting-adjusted Kaplan-Meier 5-year overall survival estimates by treatment groups. Risk table appears below graph. CRT, chemoradiation; Eso, esophagectomy; LE, local excision; Obs, observation.

Table 3 Fitted Cox model for overall survival using inverse probability of treatment weighting

Variable	Hazard ratio (95% CI)	P value
Treatment		
Local excision	1	
Esophagectomy	1.15 (1.01–1.30)	0.037
Chemoradiation	2.41 (2.09–2.78)	<0.001
Observation	3.79 (3.33–4.32)	<0.001
Age group, years		
≤50	1	
51–60	1.34 (1.08–1.68)	0.009
61–70	1.53 (1.23–1.91)	<0.001
71–80	2.07 (1.65–2.60)	<0.001
>80	3.32 (2.62–4.20)	<0.001
Sex		
Male	1	
Female	0.97 (0.87–1.08)	0.567
Race		
White	1	
Black	0.94 (0.78–1.13)	0.484
Other	0.83 (0.65–1.05)	0.121
Comorbidity score		
0	1	
1	1.34 (1.21–1.49)	<0.001
≥ 2	1.31 (1.13–1.51)	<0.001
Median income		
≥$46,000	1	
$35,000–$45,000	1.11 (1.00–1.24)	0.048
$30,000–$34,999	1.23 (1.08–1.40)	0.001
<$30,000	1.72 (1.49–1.97)	<0.001
Unknown	1.20 (0.99–1.47)	0.07
Medical insurance		
Medicare	1	
Private	0.78 (0.69–0.87)	<0.001
Medicaid	1.06 (0.85–1.31)	0.601
Other government	0.72 (0.47–1.1)	0.126
Uninsured	1.09 (0.82–1.45)	0.538
Unknown	1.27 (0.92–1.75)	0.141
Tumor location		
Lower third	1	
Middle third	1.18 (1.04–1.34)	0.009
Upper third	1.12 (0.93–1.36)	0.245
Unknown	1.02 (0.91–1.16)	0.702
Tumor grade		
1	1	
2	1.29 (1.10–1.50)	0.001
3	1.95 (1.67–2.27)	<0.001
Other/unknown	0.96 (0.82–1.13)	0.609
Facility type		
Academic	1	
Non-academic	1.21 (1.10–1.32)	<0.001
Distance from facility		
0–25 miles	1	
>25 miles	0.77 (0.70–0.85)	<0.001

Table 3 *(continued)*

HR =3.79, 95% CI: 3.33–4.32, P<0.001. When Obs was set as the reference, all treatments were again associated with significantly improved survival (data not shown). Factors found to negatively affect outcomes were older age, higher comorbidity index scores, higher tumor grade, lower income, and treatment at non-ARs (HR =1.21, 95% CI: 1.10–1.32, P<0.001).

Discussion

Patients diagnosed with stage I EC in the United States represent a heterogeneous population subject to various clinical treatment patterns. As expected per national guidelines, most patients (65%) were treated surgically with either Eso or LE. Interestingly, use of LE rose over time, and LE was associated with improved postoperative mortality rates and improved OS compared with Eso. Although esophagectomy has historically been the standard of care, endoscopic therapies have gained popularity for several reasons. Partial or total esophagectomy is considered aggressive surgery, with high rates of major morbidities as well as 30-day postoperative mortality rates ranging from 1.4% to 9.8% (19-22). Our 30-day Eso postoperative mortality rate of 2.9% is in accordance with modern-day reports and likely reflects the adoption of minimally invasive techniques (23). LE has the advantages of esophageal preservation, potentially greater quality-adjusted life years with similar long-term survival, and salvage therapy options such as re-excision or esophagectomy (4,24-26). Possible explanations for the observed survival benefit with LE over Eso in our cohort include well-selected cases with low risk of nodal metastasis, T1a disease, or higher rates of negative margin status, all of which could not be confirmed or evaluated in our analysis. Overall, the choice of surgical procedure should be made individually, with Eso the preferred option for select patients with cT1b disease or high-risk features (27,28).

Discrepancies in healthcare provided to minorities has been well documented at all stages of disease and cancer care (29,30). In our study, multiple disparities were evident with regard to ethnicity, age, and type of treatment facility. For example, Black patients were less likely to undergo any form of surgery than were White patients, regardless of median income or medical insurance. These findings are similar to other reports for Blacks and Hispanics in alternative registries such as the California Cancer registry or SEER (31,32). One particular SEER study investigating racial disparities in use of surgery for locoregional EC found a significantly lower rate of cancer-directed surgery among Blacks than Whites (40% *vs.* 53%; P<0.001), whereas rates of receiving only radiation therapy were higher among Blacks (35% *vs.* 45%) (32). We were able to provide a more thorough analysis for all group stratifications, as radiation dose restrictions and the use of concurrent chemotherapy were included in our models. Although we did not observe a significant difference in mortality based on ethnicity, other studies estimate an increase in mortality risk as high as 33% for Black patients relative to White patients with any type of cancer or all stages of EC (29).

With a median age of 67 years, elderly patients constituted a substantial portion of our population with stage I EC, which makes treatment selection more challenging as age has been considered a predictor of negative outcomes after surgery (22,33). A notable trend of decreasing odds in undergoing any surgery was found with increasing age in our group. Aside from proper assessment of patient or tumor characteristics, one explanation for this observation may be underutilization of referrals to surgical consults in this age group. Using the SEER database, Steyerberg *et al.* analyzed referral patterns for patients ≥65 years with locoregional EC and discovered that older patients were less likely to be referred to a surgeon (61% for age ≥85 years *vs.* 80% for age 65–75), which in turn led to lower rates of surgery (23% for age ≥85 years *vs.* 55% for age 65–70 yuears) (10). Elderly patients instead tend to be treated conservatively with CRT or Obs (7,34). In a previous study of patients ≥80 years old, we found that 43% received no treatment, 22% CRT, 25% LE, and 10% LE. However, surgical management, particularly LE, was associated with low postoperative mortality rates and superior outcomes relative to Obs: LE HR =0.3, 95% CI: 0.24–0.38, P<0.001; and Eso HR =0.32, 95% CI: 0.23–0.44, P<0.001 (8). Therefore, all attempts should be made to provide surgical options if possible, including a thorough risk assessment based on performance status rather than by age alone.

Another relevant discrepancy in treatment selection was the type of treating facility. Nearly two-thirds of all surgical procedures were performed in an AR institution; indeed, surgeries constituted 80% of all therapies provided in ARs. In contrast, surgeries constituted only 48% of treatments in non-ARs, and treatment at non-ARs was independently associated with worse outcomes compared with ARs (HR =1.21, 95% CI: 1.10–1.32, P<0.001). Several studies have shown a strong correlation between type of treating facility and survival, with ARs being associated with superior outcomes for patients with different types of cancer (8,35).

Lower mortality rates in ARs may be attributable to having more in-house experience and resources to handle perioperative complications or treatment-related toxicities. By NCDB definition, ARs must assess more than 500 newly diagnosed cancer cases each year and provide postgraduate medical education in at least four programs (14). Therefore, the lower 30- and 90-day postoperative mortality rates at high-volume centers versus low-volume centers is logical and warrants further evaluation when aggressive treatments are being considered at non-ARs.

We acknowledge several limitations to this study. As with any retrospective analysis, specific details regarding patient performance status, perioperative complications, and non-cancer-specific causes of death could not be assessed. Information about recurrence rates, surveillance management, and salvage therapies would also have been valuable, particularly for the surgical groups, to evaluate potential differences in outcomes after Eso versus LE. On the other hand, our study had noteworthy strengths, including the source of our data. The NCDB, now recognized as the largest clinical registry in the world with more than 34 million cancer patient records (14), is an excellent resource for comparative effectiveness research and for exploring trends in cancer care. Our cohort is relatively large and inclusive, with no age restrictions as in SEER-Medicare studies. We were also able to perform a robust analysis of health care disparities given the substantial information available on sociodemographic and facility characteristics. Finally, the IPTW method, a form of propensity score matching, was also used with the aim of reducing the effects of confounding compared with unadjusted observational studies (36).

In conclusion, our analysis suggests that discrepancies in treatment selection for patients with clinical stage I EC can lead to significant differences in long-term outcomes. Endoscopic therapy is becoming an increasingly popular alternative to esophagectomy and has been associated with lower postoperative mortality rates and the greatest survival benefit. Persistent disparities among Blacks and elderly patients were evident in our study and should continue to be addressed to provide optimal care to all patients. Finally, external validation of our findings is recommended to establish appropriate selection criteria for endoscopic therapy in the modern era.

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Footnote

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Ethical Statement: Research using the National Cancer Database was reviewed by the Institutional Review Board and granted an exemption.

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Supplementary

Table S1 Patient demographics, tumor and clinical characteristics (IPTW-adjusted)

Characteristic	Obs (n=1,159) (%)	Treatment group			Chi-square P
		CRT (n=740) (%)	LE (n=1,270) (%)	Eso (n=2,307) (%)	
Age group, years					0.764
≤50	6.79	8.73	7.07	7.2	
51–60	22.8	19.83	21.4	21.48	
61–70	32.73	30.88	31.1	32.04	
71–80	24.5	26.09	27.39	26.34	
>80	13.17	14.47	13.04	12.94	
Sex					0.545
Male	81.26	78.94	79.79	80.85	
Female	18.74	21.06	20.21	19.15	
Race					0.838
White	90.48	91.89	90.29	90.86	
Black	5.82	5.65	6.21	5.89	
Other	3.7	2.46	3.5	3.24	
Comorbidity score					0.561
0	71.69	68.79	70.96	71.5	
1	21.02	21.36	20.37	20.23	
≥2	7.29	9.85	8.67	8.27	
Median household income					0.256
<$30,000 (bottom quartile)	10.55	10.86	11.87	11.01	
$30,000–$34,999	15.93	17.3	17.55	17.77	
$35,000–$45,000	27.25	31.86	29.73	28.27	
≥$46,000 (top quartile)	40.97	36.03	37.32	38.49	
Unknown	5.29	3.95	3.53	4.47	
Medical insurance					0.221
Uninsured	1.88	1.73	3.67	2.26	
Private	36.4	34.65	34.21	34.43	
Medicaid	4.76	5.74	3.83	5.05	
Medicare	54	54.89	55.07	54.6	
Other government	1.62	1.57	1.66	1.72	
Unknown	1.34	1.42	1.56	1.94	
Tumor location (esophagus)					0.130
Lower third	67.43	70.57	67.84	71.18	
Middle third	13.74	12.27	12.17	11.7	
Upper third	3.5	4.21	5.27	3.93	
Unknown	15.33	12.96	14.71	13.19	
Facility type					0.531
Academic	52.21	51.21	51.31	53.52	
Non-academic	47.79	48.79	48.69	46.48	
Distance from facility					0.766
0–25 miles	62.09	64.18	62.28	62.09	
>25 miles	37.91	35.82	37.72	37.91	
Year of diagnosis					0.729
2004	6.46	5.45	7.90	5.82	
2005	6.41	6.97	5.25	6.39	
2006	7.03	6.98	7.53	7.66	
2007	9.75	7.58	8.50	8.46	
2008	11.64	10.55	12.09	11.65	
2009	13.48	12.04	12.82	13.50	
2010	16.05	16.15	15.39	15.35	
2011	14.14	17.03	15.06	15.18	
2012	15.03	17.25	15.46	15.99	

IPTW, inverse probability of treatment weighting; Obs, observation; CRT, concurrent chemotherapy; LE, local excision; Eso, esophagectomy.

Table S2 Insurance and median income quartiles according to race/ethnicity and treatment

Characteristics	Obs	Treatment group		
		CRT	LE	Eso
For Whites				
Number	997	646	1,166	2,162
Median household income, n (%)				
<$30,000 (bottom quartile)	103 (21.2)	101 (20.8)	89 (18.4)	192 (39.6)
$30,000–$34,999	181 (20.5)	117 (13.3)	207 (23.5)	376 (42.7)
$35,000–$45,000	277 (19.2)	185 (12.8)	341 (23.6)	642 (44.4)
≥$46,000 (top quartile)	390 (20.0)	208 (10.7)	484 (24.8)	868 (44.5)
Unknown	46 (21.9)	35 (16.7)	45 (21.4)	84 (40.0)
Medical insurance, n (%)				
Uninsured	27 (34.2)	12 (15.2)	7 (8.9)	33 (41.8)
Private	241 (13.7)	154 (8.7)	376 (21.3)	994 (56.3)
Medicaid	29 (16.7)	34 (19.5)	33 (19)	78 (44.8)
Medicare	669 (23.9)	427 (15.2)	706 (25.2)	1,000 (35.7)
Other government	14 (18)	12 (15.4)	23 (29.5)	29 (37.2)
Unknown	17 (23.3)	7 (9.6)	21 (28.8)	28 (38.4)
For Blacks				
Number	116	89	21	82
Median household income, n (%)				
<$30,000 (bottom quartile)	46 (41.1)	38 (33.9)	2 (1.8)	26 (23.2)
$30,000–$34,999	21 (30.4)	17 (24.6)	5 (7.3)	26 (37.7)
$35,000–$45,000	29 (44.6)	14 (21.5)	7 (10.8)	15 (23.1)
≥$46,000 (top quartile)	17 (32.7)	14 (26.9)	7 (13.5)	14 (26.9)
Unknown	3 (30.0)	6 (60.0)	0 (0.0)	1 (10.0)
Medical insurance, n (%)				
Uninsured	8 (44.4)	5 (27.8)	1 (5.6)	4 (22.2)
Private	30 (39.5)	18 (23.7)	8 (10.5)	20 (26.3)
Medicaid	15 (25.4)	15 (25.4)	4 (6.8)	25 (42.4)
Medicare	59 (42.8)	46 (33.3)	7 (5.1)	26 (18.8)
Other government	2 (20.0)	1 (10.0)	1 (10.0)	6 (60.0)
Unknown	2 (28.6)	4 (57.1)	0 (0.0)	1 (14.3)

Eso, esophagectomy; Obs, observation; LE, local excision; CRT, concurrent chemoradiation therapy.