

## Disparities in esophageal cancer care based on race: a National Cancer Database analysis

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**SUMMARY.** Esophageal cancer is one of the most common cancer killers in our country. The effects of racial disparities on care for esophageal cancer patients are incompletely understood. Using the National Cancer Database, we investigated racial disparities in treatment and outcome of esophageal cancer patients. The National Cancer Database was queried from 2004 to 2017. Logistic regression and survival analysis were used to determine racial differences in access, treatment and outcome. A total of 127,098 patients were included. All minority groups were more likely to be diagnosed at advanced stages versus Caucasians after adjusting for covariates (African American OR—1.64 [95% confidence interval 1.53—1.76], Hispanic OR—1.19 [1.08—1.32], Asian OR—1.78 [1.55—2.06]). After adjustment, all minorities were less likely at every stage to receive surgery. Despite these disparities, Hispanics and Asians had improved survival compared with Caucasians. African Americans had worse survival. Racial disparities for receiving surgery were present in both academic and community institutions, and at high-volume and low-volume institutions. Surgery partially mediated the survival difference between African Americans and Caucasians (HR—1.13 [1.10–1.16] and HR—1.04 [1.02–1.07], without and with adjustment of surgery). There are racial disparities in the treatment of esophageal cancer. Despite these disparities, Hispanics and Asians have improved overall survival versus Caucasians. African Americans have the worst overall survival. Racial disparities likely affect outcome in esophageal cancer. But other factors, such as epigenetics and tumor biology, may correlate more strongly with outcome for patients with esophageal cancer.

**KEY WORDS:** cancer epidemiology, cancer treatment, esophageal cancer.

### INTRODUCTION

Esophageal cancer is one of the leading causes of cancer-related deaths in the USA. Over 17,000 people in the USA die each year from esophageal cancer.<sup>1</sup> Despite advances in surgical management and chemoradiation protocols, the 5 year survival rate of esophageal cancer is still only 17%.<sup>2</sup>

Recent tragedies in this country have displayed the crisis of systemic injustice and lack of equity in our society.<sup>3</sup> Racial disparities exist in many systems in our country, including the health care system. Only 4% of all physicians in this country are African American.<sup>4</sup> Hispanic patients are frequently underrepresented as participants in clinical trials.<sup>5</sup> And many

treatment protocols are based on investigative studies which did not include patients of Asian descent.<sup>6</sup>

Minorities diagnosed with several different cancer types have been shown to have worse outcomes than Caucasians<sup>7–9</sup>. But some minority groups have traditionally experienced less complications in some disease processes compared with the rest of the population.<sup>10</sup> Although such studies have been performed for esophageal cancer, the literature has been limited in determining causes or correlations to explain these disparities in care. As such, our goals were to determine the racial disparities in access to care, treatment and outcomes in patients diagnosed with esophageal cancer. The National Cancer Database (NCDB) was queried over a 14 year period to perform this analysis.

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## METHODS

### Patients

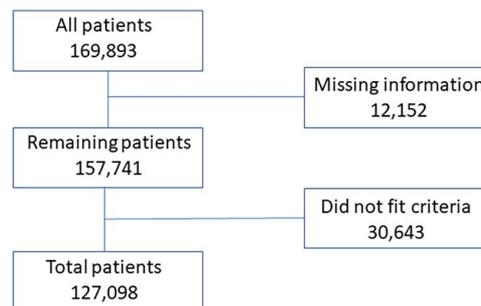
The NCDB was developed as a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society as a comprehensive database of cancer cases in the USA.<sup>11</sup> The NCDB is a clinical oncology database which acquires hospital registry data from over 15,000 Commission on Cancer-accredited facilities. The NCDB contains over 70% of all newly diagnosed cancer cases and has more than 34 million records overall. The NCDB was queried for all cases of esophageal cancer from 2004 to 2017. Only patients who had the esophagus as the primary site of their cancer were included. Patients who had overlapping primary sites were excluded. The data used in the study were derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigators.

### Variables

The following variables were collected for each patient: age, gender, ethnicity, medical insurance status, level of education, income level, Charlson-Deyo comorbidity score, distance from the patient's residence to the treating institution, urban versus rural location of patient residence, year of diagnosis, T category, N category, M category, clinical stage, pathologic stage, type of treating institution, high-volume versus low-volume esophagectomy institution, type of treatment given (surgery, chemotherapy, radiation), time from diagnosis to start of treatment and to mortality. A center was considered to be high-volume if it performed more than an average of 13 or more esophagectomies per year, as 13 was the guideline by the Leapfrog Group during the midpoint of the study.<sup>12</sup> A patient was said to have received 'any treatment' if they received surgery, chemotherapy or radiation individually or as multimodality treatment. Carcinoma in situ was considered Stage 0. Stages III and IV were considered to be advanced stage.

### Statistical methods

Demographic, cancer characteristics, facility characteristics and treatments by race/ethnicity (Caucasian, Africa Americans, Hispanic, Asians and others) were presented as means, standard deviation, median and quartile 1 and 3 for continuous variables, and as frequencies and percentage for categorical variables. A logistic regression model was used to compare the race/ethnicity disparity on stage of diagnosis adjusted for demographics and facility characteristics. We also built stratified logistic regression models by



**Fig. 1** CONSORT diagram of patients.

stage to assess the race/ethnicity disparity on various treatments with the same adjustments. Interactions between race/ethnicity and facility characteristics on the outcomes of treatment were tested. To examine the race/ethnicity disparity on survival, unadjusted survival rates were estimated by using Kaplan–Meier method and compared with the log-rank test. Multivariate Cox Proportional Hazard models were used to estimate hazard ratios adjusted for demographics and facility characteristics. To assess the effect of stage at diagnosis and treatments on race/ethnicity disparity of survival, we added these variables step by step to the Cox proportional hazard model. All patients were censored at the last contact date or at the end of study (December 31, 2019). The proportional hazard assumption was evaluated first by visual inspection of the Kaplan–Meier curve and then by adding the interaction between race and log (time) to the model and checking for significance. In both the Kaplan–Meier analysis and the Cox proportional hazards model, patients diagnosed in 2017 were excluded due to not having follow-up information. All analyses were conducted using SAS 9.4 (Cary, NC).

## RESULTS

### Demographics

A total of 169,893 patients were available in the database for review. After exclusion of patients with missing data and those that did not fit criteria, 127,098 patients were included in the analysis (Fig. 1).

Table 1 lists patient demographics. The age of African American patients ( $63.7 \pm 10.4$  years) and Hispanic patients ( $64.9 \pm 11.5$  years) tended to lower than Caucasian patients ( $66.9 \pm 10.9$  years) and Asian patients ( $66.9 \pm 11.0$  years). The highest proportion of female patients was among African Americans (31.8%), followed by Asians (24.9%), Hispanics (20.0%) and Caucasians (19.7%). Distance from the treating institution was lowest for African Americans ( $16.2 \pm 64.4$  miles), followed by Hispanics ( $22.7 \pm 82.9$  miles), Asians ( $24.0 \pm 160.1$  miles) and Caucasians ( $34.2 \pm 109.3$  miles). The highest per-

**Table 1** Patient demographics

	White (N = 107,256)	African American (N = 11,605)	Hispanic (N = 4241)	Asian (N = 2041)	Other (N = 1955)
<b>Age at diagnosis</b>					
Mean ± SD (years)	66.9 ± 10.9	63.7 ± 10.4	64.9 ± 11.5	66.9 ± 11.0	65.8 ± 10.9
Median, 25th–75th percentile (years)	67 (59–75)	63 (56–71)	65 (56–73)	67 (59–75)	66 (58–74)
<50	6125 (5.7%)	938 (8.1%)	415 (9.8%)	130 (6.4%)	130 (6.7%)
50–59	22,114 (20.6%)	3378 (29.1%)	1036 (24.4%)	400 (19.6%)	445 (22.8%)
60–69	34,704 (32.4%)	3973 (34.2%)	1297 (30.6%)	653 (32.0%)	634 (32.4%)
70–79	29,088 (27.1%)	2442 (21.0%)	976 (23.0%)	592 (29.0%)	516 (26.4%)
80+	15,225 (14.2%)	874 (7.5%)	517 (12.2%)	266 (13.0%)	230 (11.8%)
<b>Gender</b>					
Male	86,145 (80.3%)	7916 (68.2%)	3393 (80.0%)	1533 (75.1%)	1520 (77.8%)
Female	21,111 (19.7%)	3689 (31.8%)	848 (20.0%)	508 (24.9%)	435 (22.3%)
<b>Urban/Rural</b>					
Metro	86,437 (80.6%)	10,146 (87.4%)	3983 (93.9%)	1986 (97.3%)	1575 (80.6%)
Urban, non-metro	18,570 (17.3%)	1299 (11.2%)	241 (5.7%)	53 (2.6%)	321 (16.4%)
Rural	2249 (2.1%)	160 (1.4%)	17 (0.4%)	2 (0.1%)	59 (3.0%)
<b>Primary Payor</b>					
Not insured	2734 (2.6%)	943 (8.1%)	377 (8.9%)	134 (6.6%)	69 (3.5%)
Private	38,100 (35.5%)	2660 (22.9%)	1301 (30.7%)	703 (34.4%)	677 (34.6%)
Medicaid	5485 (5.1%)	2485 (21.4%)	641 (15.1%)	327 (16.0%)	182 (9.3%)
Medicare	58,858 (54.9%)	5285 (45.5%)	1871 (44.1%)	865 (42.4%)	912 (46.7%)
Other Gov	2079 (1.9%)	232 (2.0%)	51 (1.2%)	12 (0.6%)	115 (5.9%)
<b>Income</b>					
Q1	14,165 (13.2%)	5716 (49.3%)	1154 (27.2%)	152 (7.5%)	345 (17.7%)
Q2	25,122 (23.4%)	2488 (21.4%)	949 (22.4%)	322 (15.8%)	387 (19.8%)
Q3	30,798 (28.7%)	1991 (17.2%)	1095 (25.8%)	505 (24.7%)	505 (25.8%)
Q4	37,171 (34.7%)	1410 (12.2%)	1043 (24.6%)	1062 (52.0%)	718 (36.7%)
<b>Charlson-Deyo Score</b>					
0	76,252 (71.1%)	8278 (71.3%)	3068 (72.3%)	1580 (77.4%)	1426 (72.9%)
1	21,801 (20.3%)	2261 (19.5%)	821 (19.4%)	369 (18.1%)	366 (18.7%)
2	6217 (5.8%)	686 (5.9%)	214 (5.1%)	63 (3.1%)	110 (5.6%)
3+	2986 (2.8%)	380 (3.3%)	138 (3.3%)	29 (1.4%)	53 (2.7%)
<b>Region</b>					
Midwest	32,013 (29.9%)	2423 (20.9%)	409 (9.6%)	209 (10.2%)	478 (24.5%)
Northeast	25,786 (24.0%)	2094 (18.0%)	1006 (23.7%)	558 (27.3%)	496 (25.4%)
South	33,908 (31.6%)	6603 (56.9%)	1471 (34.7%)	328 (16.1%)	467 (23.9%)
West	15,549 (14.5%)	485	1355 (32.0%)	946 (46.4%)	514 (26.3%)
<b>Distance from patient address to hospital</b>					
Mean ± SD (miles)	34.2 ± 109.3	16.2 ± 64.4	22.7 ± 82.9	24.0 ± 160.1	66.3 ± 211.4
Median, 25th–75th percentile (miles)	11.8 (4.9–29.4)	5.9 (2.7–14.0)	7.0 (3.2–15.3)	6.3 (3.0–12.1)	15.0 (5.2–49.8)
<b>Facility type</b>					
Community Cancer Program	9830 (9.2%)	850 (7.3%)	323 (7.6%)	182 (8.9%)	109 (5.6%)
Comprehensive Community Cancer Program	42,390 (39.5%)	3777 (32.6%)	1370 (32.3%)	590 (28.9%)	492 (25.2%)
Academic/Research	41,803 (39.0%)	5607 (48.3%)	2029 (47.8%)	1082 (53.0%)	1116 (57.1%)
Integrated Network Cancer Program	13,233 (12.3%)	1371 (11.8%)	519 (12.2%)	187 (9.2%)	238 (12.2%)
<b>Facility Volume</b>					
<13 per year	60,840 (56.7%)	7085 (61.1%)	2660 (62.7%)	1097 (53.8%)	783 (40.1%)
13 or greater per year	46,416 (43.3%)	4520 (39.0%)	1581 (37.3%)	944 (46.3%)	1172 (60.0%)
<b>Overall Stage</b>					
0/1	21,560 (20.1%)	1,563 (13.5%)	710 (16.7%)	302 (14.8%)	428 (21.9%)
2	22,989 (21.4%)	2402 (20.7%)	860 (20.3%)	441 (21.6%)	395 (20.2%)
3	26,534 (24.7%)	3351 (28.9%)	1104 (26.0%)	690 (33.8%)	515 (26.3%)
4	36,173 (33.7%)	4289 (37.0%)	1567 (37.0%)	608 (29.8%)	617 (31.6%)
<b>Had Treatment</b>					
No	18,098 (16.9%)	2475 (21.3%)	1019 (24.0%)	422 (20.7%)	450 (23.0%)
Yes	89,158 (83.1%)	9130 (78.7%)	3222 (76.0%)	1619 (79.3%)	1505 (77.0%)
<b>Time from diagnosis to treatment, mean ± SD (days)</b>	36.9 ± 34.1	39.8 ± 39.4	40.9 ± 37.2	37.4 ± 36.6	38.9 ± 36.0
<b>Time from diagnosis to treatment, median, 25th–75th percentile (days)</b>	32 (19–47)	32 (18–51)	33 (18–53)	31 (18–47)	31 (18–50)
<b>Radiation</b>					
No	46,145 (43.0%)	4483 (38.6%)	2068 (48.8%)	794 (38.9%)	1017 (52.0%)
Yes	61,111 (57.0%)	7122 (61.4%)	2173 (51.2%)	1247 (61.1%)	938 (48.0%)
<b>Surgery</b>					
No	69,462 (64.8%)	9711 (83.7%)	3078 (72.6%)	1512 (74.1%)	1300 (66.5%)
Yes	37,794 (35.2%)	1894 (16.3%)	1163 (27.4%)	529 (26.0%)	655 (33.5%)
<b>Chemotherapy</b>					
No	40,230 (37.5%)	4596 (39.6%)	1794 (42.3%)	785 (38.5%)	953 (48.8%)
Yes	67,026 (62.5)	7009 (60.4%)	2447 (57.7%)	1256 (61.5%)	1002 (51.2%)

**Table 2** Odds of being diagnosed at an advanced stage versus Stage 0/1 for each race

	Stage 2 versus 0/1	Stage 3 versus Stage 0/1	Stage 4 versus Stage 0/1	P-value
Caucasian	Reference	Reference	Reference	Reference
African American	1.43 (1.33–1.54)	1.62 (1.51–1.74)	1.52 (1.42–1.63)	<0.01
Hispanic	1.16 (1.04–1.29)	1.18 (1.07–1.31)	1.21 (1.09–1.33)	<0.01
Asian	1.42 (1.22–1.65)	1.79 (1.55–2.06)	1.20 (1.03–1.39)	<0.01

centage of patients in the lowest economic quartile was among African Americans (49.3%), followed by Hispanics (27.2%), Caucasians (13.2%) and Asians (7.5%).

The groups most likely to be treated at academic/research institutions were Asians (53.0%), followed by African Americans (48.3%), Hispanics (47.8%) and Caucasians (39.0%). Asians were the group most likely to be treated at high-volume centers (46.3%), followed by Caucasians (43.3%), African Americans (39.0%) and Asians (37.3%).

### Stage at diagnosis

All minorities were more likely to be diagnosed at advanced stages compared with Caucasians (Table 2). The distribution of Stage 0/1, 2, 3 and 4 disease for African Americans was 13.5%, 20.7%, 28.9% and 37.0%. The distribution of Stage 0/1, 2, 3 and 4 disease for Hispanics was 16.7%, 20.3%, 26.0% and 37.0%. The distribution of Stage 0/1, 2, 3 and 4 disease for Asians was 14.8%, 21.6%, 33.8% and 29.8%. The distribution of Stage 0/1, 2, 3 and 4 disease for Caucasians was 20.1%, 21.4%, 24.7% and 33.7%. Even when adjusted for other demographics and facility characteristics, all minorities had significantly increased odds of being diagnosed at Stages 2, 3 and 4 compared with Caucasians (Table 2).

### Treatment pattern

The likelihood of receiving surgery is shown in Figure 2 for every race at every stage. Minorities tended to be less likely to receive surgery at every stage compared with Caucasians. For Stage 0/1, 2, 3 and 4 disease, African Americans had hazard ratios of 0.34, 0.39, 0.33 and 0.46, respectively, of receiving surgery compared with Caucasians. For Stage 0/1, 2, 3 and 4 disease, Hispanics had hazard ratios of 0.72, 0.90, 0.63 and 0.99, respectively, of receiving surgery compared with Caucasians. For Stage 0/1, 2, 3 and 4 disease, Asians had hazard ratios of 0.46, 0.72, 0.49 and 1.02, respectively, of receiving surgery compared with Caucasians. In particular, African Americans were the least likely to be offered surgery. Only 16.3% of African Americans received surgery, compared with 33.1% of the overall cohort.

**Table 3** Survival hazard ratios after adjustment for stage and stage + surgery

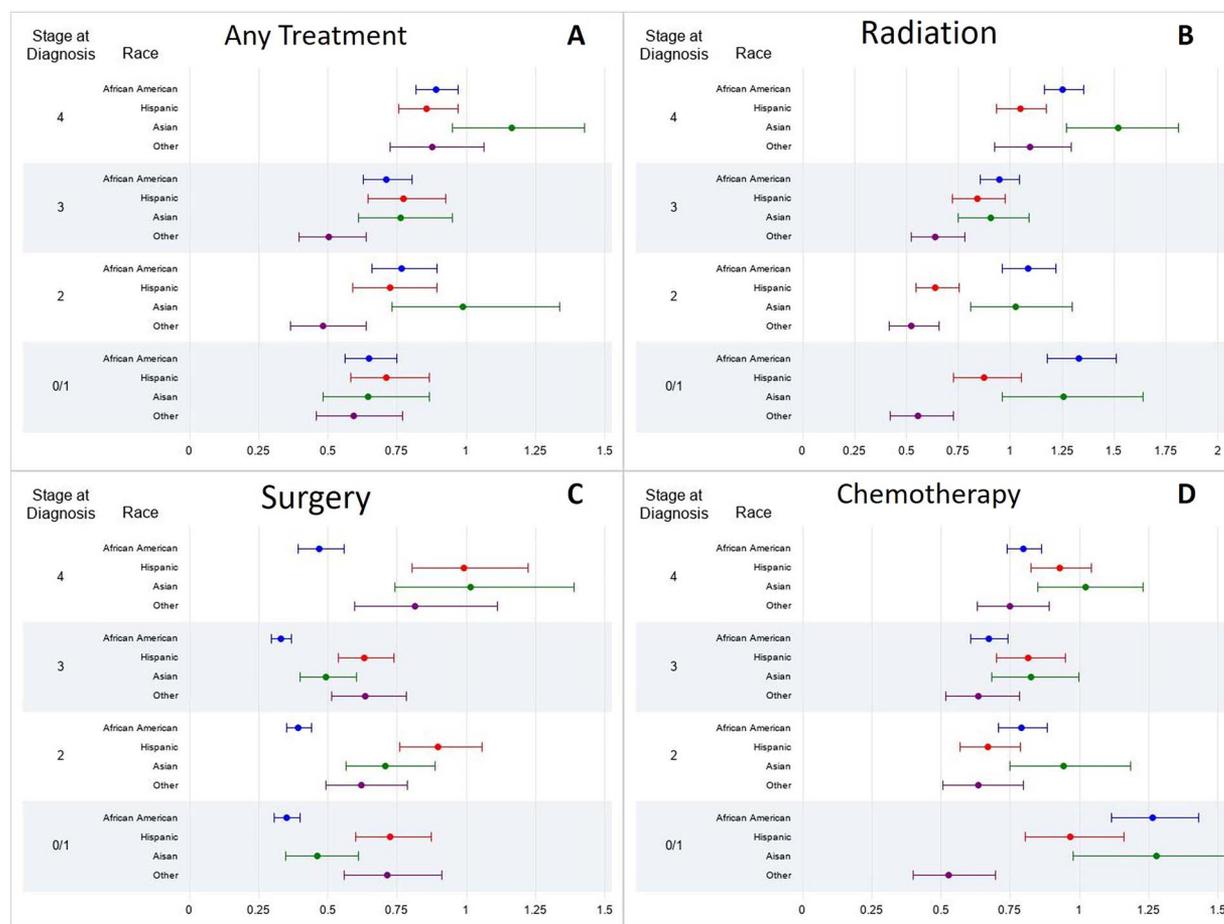
Ethnicity	Hazard ratio adjusted for stage	Hazard ratio adjusted for stage and surgery
Caucasian	Reference	Reference
African American	1.13 (1.10–1.15)	1.04 (1.02–1.07)
Hispanic	0.84 (0.81–0.88)	0.82 (0.79–0.85)
Asian	0.83 (0.78–0.87)	0.78 (0.74–0.83)
Other	0.96 (0.91–1.01)	0.93 (0.88–0.98)

### Overall survival

After adjusting for survival and treatment pattern, African Americans had a statistically significant decrease in survival compared with Caucasians (hazard ratio 1.04, 1.02–1.07) and overall had the worst survival. In comparison, Hispanics (hazard ratio 0.82, 0.79–0.85) and Asians (hazard ratio 0.78, 0.74–0.83) had statistically significant improvements in survival after adjusting for stage and treatment pattern (Fig. 3). When adjusting only for stage, African Americans still had an overall worse survival versus Caucasians (hazard ratio 1.13, 1.10–1.15, Table 3).

### DISCUSSION

Our study revealed that there were racial disparities in treatment pattern and outcome for patients with esophageal cancer. Minorities tended to be diagnosed at advanced stages. This trend has been seen in numerous other disease processes<sup>13–15</sup>. There are multiple potential reasons for this disparity, and opportunities to reduce these inequities. Firstly, screening rates for many cancers are lower in minorities<sup>16,17</sup>. Patients eligible for screening for esophageal cancer include men or women with chronic symptoms (greater than 5 years) of gastroesophageal reflux disease (GERD) and two or more risk factors for Barrett's esophagus or esophageal adenocarcinoma. Risk factors included Caucasian race, age  $\geq 50$  years, current or prior history of smoking, central obesity as defined as a waist circumference greater than 88 cm, waist to hip ratio greater than 0.8 or a family history of Barrett's esophagus or esophageal adenocarci-



**Fig. 2** Odds of treatments being given based on race after adjustment for covariates. African Americans and Hispanics had lower odds of any treatment being given at all stages.

noma.<sup>18</sup> A focused intervention improving awareness of the benefits of screening in minority communities would help to diagnose disease earlier. This awareness campaign can target both the community and health care providers in these areas. Although the medical community strives to treat all patients equally, cultural stereotypes and unconscious biases may contribute to health disparities.<sup>19</sup> These awareness campaigns will require counseling of providers as well as patients to be effective.

Secondly, there were treatment disparities based on race that were evident in our study. African Americans were less likely to receive surgery at all stages. Although tumor biology likely affected outcome, the disparity in receiving surgery affected outcome as well. Other studies have shown that African Americans are less likely to receive surgery for several disease processes, and that when African Americans receive surgery the disease process is more advanced.<sup>20</sup> There are multiple reasons for this disparity in receiving surgery. Unfortunately, there are large segments of the African American population which are hesitant to seek medical care and have suspicion of the medical community<sup>21,22</sup>. In addition, previous literature has shown that providers are less likely to offer surgery to

minorities when indicated.<sup>23</sup> Educating providers and patients about all treatment options is likely to reduce this disparity in receiving surgery.

An interesting finding in our study was that Hispanic and Asian patients had a better survival overall, despite disparities in care. Our study is novel in that we showed that for some disease processes like esophageal cancer, the biology of the disease may be more critical than the access to treatment. Esophageal cancer is associated with a very poor prognosis compared with other solid organ tumors. The tumor biology and epigenetic factors of esophageal cancer may impact outcome, but future studies are required to examine this correlation.

This trend has been described previously in Hispanic patients as the ‘Hispanic paradox’ phenomenon<sup>24,25</sup>. Multiple genes have been identified which are related to esophageal cancer development and are differentially expressed in various races. Further research may identify that some of these differentially expressed genes are related to racial differences in outcome.

Our study defined ‘high-volume’ based on the number of yearly esophagectomies determined by The Leapfrog Group. Multiple studies have shown

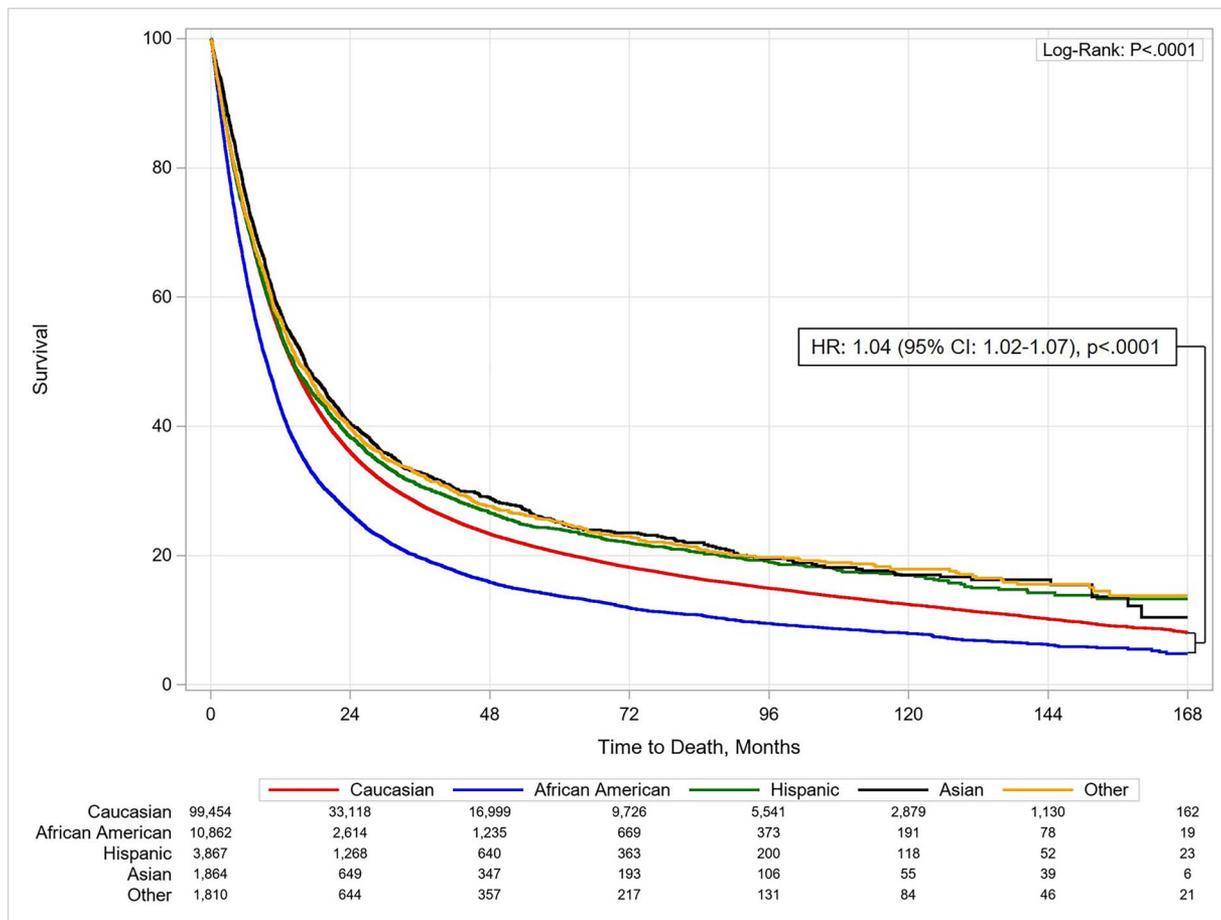


Fig. 3 Survival by race.

that as a center performs more surgeries, their outcomes improve. But previous studies have not examined whether high-volume centers provide more equitable care than low-volume centers. Our study showed that the disparities in treatment patterns were present at both high-volume and low-volume institutions. Despite having more familiarity with esophagectomies, high-volume centers still offered surgery less frequently to minorities. Similarly, disparities in treatment were present at academic/research and community institutions. This disparity exists for reasons other than familiarity with esophageal cancer, and a solution will have to target all types of institutions to be effective.

Analysis of disparities in treatment pattern can possibly be complicated by interactions of social determinants with each other<sup>26,27</sup>. Minorities are more likely to be in lower income levels and are more likely to be uninsured.<sup>28</sup> We attempted logistic regression analysis to determine the impact of individual factors on treatment pattern and outcome, but there are likely relationships between some social determinants which are not fully measured in the database.

There were several limitations to our study. Although the NCDDB is quite robust, there were no cancer-specific survival data available. Secondly, the information on chemotherapy and radiation lacked details such as dose and regimen used. Thirdly, some sociodemographic information such as income and education levels was measured at the zip code level and not for each individual. Fourthly, although the overall stage was present in most cases, the specific TNM categories were missing in many situations. Additionally, complete histologic data were not available and could have had some impact on the interpretation of the data. Despite these limitations, the vast amount of data and large number of patients made this study useful and revealing.

Esophageal cancer is a morbid disease with a relatively low 5 year survival. There are significant disparities in treatment patterns in this country based on race. Despite these disparities, Hispanic and Asian patients have better outcomes. As such, it appears that tumor biology and epigenetic phenomena impact outcome meaningfully in esophageal cancer. Future efforts to reduce treatment disparities should focus on patients and providers. In addition, future research

should search for race-related differential gene expression which may explain differences in outcome related to race.

## AUTHOR CONTRIBUTIONS

Conceptualization: Ikenna C. Okereke, Jordan Westra, Douglas Tyler, Yong-Fang Kuo, Suzanne Klimberg, Rohit Venkatesan; Formal analysis and data curation: Jordan Westra, Daniel Jupiter, Yong-Fang Kuo, Kaelyn Brooks; Supervision: Ikenna C. Okereke; Writing—original draft and editing: Ikenna C. Okereke, Jordan Westra, Douglas Tyler, Daniel Jupiter, Yong-Fang Kuo.

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