Published in final edited form as:

Ann Surg Oncol. 2013 April ; 20(4): 1136–1141. doi:10.1245/s10434-012-2807-3.

Racial disparities in esophageal cancer outcomes

Sha'Shonda L. Revels, MD MA, Arden M. Morris, MD MPH, Rishindra M. Reddy, MD, Clifford Akateh, BS, and Sandra L. Wong, MD MS

Department of Surgery, University of Michigan, Ann Arbor

Abstract

Introduction—Racial disparities in outcomes have been documented among patients with esophageal cancer. The purpose of this study is to identify mechanisms for ethnicity/race-related differences in the use of cancer-directed surgery and mortality.

Methods—Data from the Surveillance, Epidemiology and End Results (SEER) program were used to evaluate non-hispanic black, non-hispanic white and hispanic patients diagnosed with non-metastatic esophageal cancer (squamous cell carcinoma (SCC) or adenocarcinoma) from 2003–2008. Age, marital status, stage, histology and location were examined as predictors of receipt of surgery and mortality in multivariate analyses.

Results—6,737 patient files (84% white, 10% black, 6% hispanic) were analyzed. Black and hispanic patients were more likely than whites to have SCC (86% vs. 41% vs. 26%, respectively; $p<0.001$) and lesions in the mid-esophagus (58% vs. 38% vs. 26%, respectively; $p<0.001$). Blacks and hispanics were less likely to undergo esophagectomy (adjusted OR 0.49, 95%CI=0.39–0.60 and 0.72, 95%CI=0.57–0.90). We noted significant variations in esophagectomy rates among patients with mid-esophageal cancers; 15% of blacks underwent esophagectomy compared to 22% of hispanics and 29% of whites ($p<0.001$). Black and hispanic patients had a higher unadjusted risk of mortality (HR 1.38, 95%CI=1.25–1.52 and 1.20, 95%CI=1.05–1.37). However, differences in mortality were no longer significant after adjusting for receipt of surgery.

Conclusion—Disparities in esophageal cancer outcomes are associated with the lower use of cancer-directed surgery. To decrease disparities in mortality it will be necessary to understand and target underlying causes of lower surgery rates in non-white patients and develop interventions, especially for mid-esophageal cancers.

Introduction

The incidence of esophageal cancer has been increasing over the past two decades with over 17,000 new diagnoses and over 15,000 deaths in the US annually.[1] Overall, advances in multimodal treatment, including chemotherapy, radiation and surgical techniques have improved esophageal cancer outcomes. However, not all populations have benefited from these treatment strategies, and survival continues to be poorer among minority patients. [2–5] Nationally, the 5-year survival in black patients with localized esophageal cancer is

21.3% compared to 39.6% in whites.[6] While the racial and ethnic disparity in esophageal cancer outcomes has been well-documented, the underlying mechanisms are not well described.

Race- and ethnicity-related variation in the receipt of evidence based processes of care is a common explanation for disparate outcomes. [7–9] For many cancer types, race and ethnicity are significant predictors of non-operative management among patients with potentially resectable tumors.[7,10–12] Lower socioeconomic status, higher burden of comorbid conditions, and differential access to surgical specialists have been associated with failure to undergo cancer-directed surgery.[13] However, accounting for patient level factors and access-related issues have failed to fully explain the underuse of surgical resection and the excess mortality observed in non-white patients with esophageal cancer.[3]

The purpose of this study was to identify underlying mechanisms of racial and ethnic disparities in esophageal cancer treatment and outcomes. First, we explored the relationship between race, ethnicity and the receipt of cancer-directed surgery while adjusting for patient and tumor factors. Second, we examined the roles of race, ethnicity and cancer directed-surgery in overall survival.

Methods

Data

We used the Surveillance Epidemiology and End Results (SEER) database of the National Cancer Institute to identify the study cohort. The SEER 17 program of the National Cancer Institute is a cancer-specific database that contains patient demographics and information related to tumor stage, location and surgical treatment. At the time of the study, SEER registries covered eleven states, and seven county-based areas within an additional three states, and represented 28% of the United States population. This population-based cohort is considered a representative racial and socioeconomic sample of the United States.[9]

Study Population

We identified non-hispanic black, non-hispanic white, and hispanic patients ages 18–85 who were diagnosed with local and regional (non-metastatic) esophageal cancer between January 1, 2003 and December 31, 2008. Patients with squamous cell (SCC) and adenocarcinoma, histologies which comprise 95% of all esophageal cancers, were included. Patients with distal and mid- esophageal cancers were included in the analysis. Surgical resection, either alone or combined with chemoradiation, is the preferred treatment for this population. Patients with cervical (proximal) cancers were excluded, because surgery is rarely indicated (n=817). Patients were also excluded if they had histology other than SCC or adenocarcinoma (n=1,214). Patients with an unknown surgical status were also excluded from the analysis (n=64).

Study Variables

The primary exposure variable was non-hispanic black, non-hispanic white or hispanic ethnicity/race. The primary outcome of the study was receipt of cancer-directed surgery

(esophagectomy), as coded in the *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM). Palliative, local ablative and/or diagnostic procedures were not included in the definition of cancer-directed surgery. The secondary outcome was mortality obtained from the SEER files. Patient demographics (age at diagnosis, gender and marital status) and tumor characteristics (stage, location and histology) were included in the analysis.

Statistical Analysis

Univariate analysis, performed with the chi-squared test for categorical variables and analysis of variance (ANOVA) for continuous variables, was used to compare racial and ethnic differences in patient demographics and tumor characteristics. We used logistic regression to evaluate the relationship between race, ethnicity and receipt of cancer-directed surgery. The model was adjusted for patient and tumor characteristics as potential confounders.

Cox proportional hazards regression was used to evaluate the relationship between race, ethnicity and mortality. The model was sequentially adjusted for patient factors, tumor factors and receipt of cancer-directed surgery. Survival time was calculated as the numbers of days from cancer diagnosis until death. Patients who were alive after December 31, 2008 were censored.

All tests of statistical significance were two-sided, and statistical significance was defined as $p < 0.05$. All analyses were performed with STATA 12 (StataCorp, College Station, TX). This project was exempt from Institutional Review Board examination.

Results

Patient Characteristics

The analytic cohort consisted of 6,737 patients. Among these, 5,652 were non-hispanic white, 700 non-hispanic black and 385 hispanic. Black patients were significantly younger at the time of diagnosis compared to hispanic and white patients (63.7 v 66.1 v 67.2 years of age, $p < 0.001$, respectively), and black patients were more likely to be single at the time of diagnosis ($p < 0.001$; Table 1). We identified significant racial differences in tumor histology and location (Table 1); however, there were no racial or ethnic differences in cancer stage at the time of diagnosis. Black and hispanic patients were considerably more likely to have SCC histology compared to white patients (85.9% v 40.8% v 26.1%, respectively $p < 0.001$; Table 1). Black and hispanic patients were also more likely to have mid-esophageal cancers compared to whites (58.1% v 37.7% v 21.4%, $p < 0.001$; Table 1). Overall, there was a significant relationship between histology and tumor location with 61.1% of squamous cell cancers located in the mid-esophagus compared to 8.8% of adenocarcinomas ($p < 0.001$; Table 2).

Use of cancer-directed surgery

The unadjusted odds of undergoing esophagectomy were significantly lower for black and hispanic patients, compared to whites (Odds Ratio [OR] = 0.33, 95% Confidence interval

[CI] = 0.28–0.40 and OR=0.67, 95% CI= 0.55–0.84, respectively; Table 3). After adjusting for patient and tumor characteristics, black and hispanic patients remained significantly less likely to undergo an esophagectomy (OR= 0.48, 95% CI= 0.39–0.60 and OR= 0.71, 95% CI= 0.56–0.90, respectively; Table 3). Regardless of race or ethnicity, the odds of surgical resection were significantly lower in patients with SCC (OR= 0.57, 95% CI= 0.49–0.65), and patients with cancers located in the mid-esophagus (OR=0.58, 95% CI= 0.50–0.67).

We also noted an ethnicity/race effect within tumor location and histology categories (Figure 1). Rates of resection for patients with mid-esophageal cancers were low for all three race/ethnicity groups with both SCC and adenocarcinoma; however differences were particularly pronounced among black patients with adenocarcinoma. Only 15% of black patients with mid-esophageal cancers underwent esophagectomy compared to 23% of hispanics and 28.9% of whites ($p<0.001$; Figure 2). The difference is slightly less pronounced for patients with distal esophageal cancers; 32.4% of blacks underwent cancer-directed surgery compared to 45% of hispanics and 50.8% of whites ($p<0.001$; Figure 2).

Relationship between race, ethnicity and mortality

Black and hispanic patients had a significantly higher unadjusted hazard of mortality than whites (Hazard ratio [HR] = 1.38, 95% CI= 1.25–1.52 and HR=1.20, 95% CI= 1.05–1.37, respectively; Table 4). After controlling for patient and tumor characteristics, racial and ethnic differences in mortality remained significant (HR =1.13, 95% CI 1.02–1.24 and HR=1.17, 95% CI 1.02–1.34, respectively; Table 4). However, differences in mortality were no longer apparent after accounting for the receipt of cancer-directed surgery.

Discussion

Using population-based data, we demonstrated race- and ethnicity-related variation in esophageal cancer histology and location. Non-white patients were significantly more likely to have tumors with squamous cell histology and tumors located in the middle esophagus compared to white patients. Moreover, we found that resection rates varied widely based upon race, ethnicity, histology and tumor location. Non-white race, SCC histology and mid-esophageal cancer location were independent predictors of non-operative management. As a result, racial and ethnicity- related disparities in resection-rates were much more pronounced in black and hispanic patients due the preponderance of SCC histology and mid-esophageal lesions. The underuse of cancer-directed surgery in non-white patients contributed to higher mortality rates among this population.

Consistent with published reports we found a preponderance of SCC histology among minority patients. [14, 15] Risk factors for SCC are different from those related to adenocarcinoma and include sources of chronic irritation, inflammation and oxidative damage. Related behavioral risk factors for SCC, such as diets low in fresh fruits and vegetables, diets high in red meat, micronutrient deficiencies and heavy alcohol and tobacco use, are widely correlated with low socioeconomic status. [16–17] We confirmed a strong relationship between tumor histology and tumor location. Overall, SCC cancers were significantly more likely to be located in the middle esophagus while adenocarcinoma was more likely to be identified in distal esophagus. Our findings are consistent with historical

trends, as the incidence of adenocarcinoma correlates with the increasing incidence of distal-esophageal tumors.[2,18]

In addition, we found that esophagectomy rates varied independently by race/ethnicity, histology, and tumor location. Prior studies have described race-related disparities in esophagectomy rates; however the underlying processes were not well delineated. Separate analyses of the SEER and SEER-Medicare databases, have shown that surgery is underutilized among black patients with potentially resectable esophageal cancer. [5–10] The current study confirms that resection rates are lower among non-white patients. It is plausible that disparities in resection rates are more pronounced in black and hispanic patients *because* of the higher proportion of SCC and therefore mid-esophageal tumors among these groups. Non-white patients may have decreased access to centers with sufficient volume and experience with the complex operations required for mid-esophageal lesions. [19] Granular examination of physician attitudes, behaviors and referral patterns may inform how to change practice patterns and assure that non-white patients are referred to surgeons for appropriate management.

Finally, previous studies have documented racial differences in the health outcomes of patients with esophageal cancer.[2,4,5,10] We found that there were no race/ethnicity-associated differences in tumor stage and that disparities in survival disappeared after adjusting for receipt of esophagectomy. Taken together, these findings imply that underuse of cancer-directed surgery in non-white patients contributes substantially to higher mortality rates.

We must acknowledge that racial and ethnicity-related differences in the use of potentially life-saving surgery persisted even after accounting for tumor histology and location illustrating that disparities in resection rates are in fact multifactorial. Previous studies have reported that non-white patients were substantially less likely to go to the operating room despite risk-adjustment for patient, tumor and hospital level characteristics. [8–9, 20] Disparities in resection rates and survival may also be related to the quality of care received and race-related differences in the patient-physician relationship and systems-based coordination of care issues. [8, 21] These issues must be clarified to better understand underlying causes for low esophagectomy rates in non-white patients with potentially resectable disease.

Our study had several limitations which must be noted. First, our dataset did not include important patient-level determinants of cancer survival including comorbidities, patient-level socioeconomic status, insurance coverage, information regarding the treating facilities, or information about the use of systemic therapies. Important patient and hospital level characteristics may preclude cancer resection such as coexisting illnesses or lack of access to specialists, which deserves further investigation as a potential area for intervention. Second, the study does not address patient-physician interactions or provide information regarding racial variation in treatment decision making. Patient-physician relationships are no doubt crucial to provision of care and the current data support further study of these mechanisms.

In summary, using population-based data, we demonstrate that race and ethnicity are associated with esophageal cancer histology and location, which in turn are related to cancer-directed surgery. The use of cancer-directed surgery is associated with longer overall survival in patients with early stage esophageal cancer and we have shown that racial and ethnic differences in esophageal cancer survival are ameliorated after controlling for receipt of cancer-directed surgery. The failure of non-whites to undergo cancer-directed surgery is an important public health and policy issue. To decrease disparities in esophageal cancer outcomes, it will be necessary to better understand underlying causes for low esophagectomy rates in non-white patients and to develop interventions that improve curative surgery rates for mid-esophageal cancer.

Acknowledgements

This work is supported by funding from the University of Michigan Surgical Oncology Research Training Program (2T32 CA009672-21 National Institutes of Health/National Cancer Institute to SLR) and the Michigan Institute for Clinical & Health Research (UL1RR024986 National Institutes of Health/National Center for Research Resources to SLR and SLW).

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin.* 2012; 62(1):10–29. [PubMed: 22237781]
2. Baquet CR, Commiskey P, Mack K, Meltzer S, Mishra SI. Esophageal cancer epidemiology in blacks and whites: racial and gender disparities in incidence, mortality, survival rates and histology. *J Natl Med Assoc.* 2005; 97(11):1471–1478. [PubMed: 16334494]
3. Miller JA, Rege RV, Ko CY, Livingston EH. Health care access and poverty do not explain the higher esophageal cancer mortality in African Americans. *Am J Surg.* 2004; 188(1):22–26. [PubMed: 15219480]
4. Greenstein AJ, Litle VR, Swanson SJ, Divino CM, Packer SP, McGinn TG, Wisnivesky JP. Racial disparities in esophageal cancer treatment and outcomes. *Ann Surg Oncol.* 2008; 15(3):881–888. [PubMed: 17987341]
5. Steyerberg EW, Earle CC, Neville BA, Weeks JC. Racial differences in surgical evaluation, treatment, and outcome of locoregional esophageal cancer: a population-based analysis of elderly patients. *J Clin Oncol.* 2005; 23(3):510–517. [PubMed: 15659496]
6. [accessed January 11,2012] Cancer of the Esophagus: 5-Year Relative and Period Survival (Percent) by Race, Sex, Diagnosis Year, Stage and Age. Surveillance, Epidemiology, and End Results (SEER) Program. Available: http://seer.cancer.gov/csr/1975_2008/results_single/sect_08_table.08.pdf.
7. Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. *N Engl J Med.* 1999; 341(16):1198–1205. [PubMed: 10519898]
8. Morris AM, Rhoads KF, Stain SC, Birkmeyer JD. Understanding racial disparities in cancer treatment and outcomes. *J Am Coll Surg.* 2010; 211(1):105–113. [PubMed: 20610256]
9. Morris AM, Billingsley KG, Hayanga AJ, Matthews B, Baldwin LM, Birkmeyer JD. Residual treatment disparities after oncology referral for rectal cancer. *J Natl Cancer Inst.* 2008; 100(10):738–744. [PubMed: 18477800]
10. Paulson EC, Ra J, Armstrong K, Wirtalla C, Spitz F, Kelz RR. Underuse of esophagectomy as treatment for resectable esophageal cancer. *Arch Surg.* 2008; 143(12):1198–1203. discussion 1203. [PubMed: 19075172]
11. Mathur AK, Osborne NH, Lynch RJ, Ghaferi AA, Dimick JB, Sonnenday CJ. Racial/ethnic disparities in access to care and survival for patients with early-stage hepatocellular carcinoma. *Arch Surg.* 2010; 145(12):1158–1163. [PubMed: 21173289]

12. Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS. National failure to operate on early stage pancreatic cancer. *Ann Surg*. 2007; 246(2):173–180. [PubMed: 17667493]
13. Birkmeyer NJ, Gu N, Baser O, Morris AM, Birkmeyer JD. Socioeconomic status and surgical mortality in the elderly. *Med Care*. 2008; 46(9):893–899. [PubMed: 18725842]
14. Merkow RP, Bilimoria KY, McCarter MD, et al. Effect of histologic subtype on treatment and outcomes for esophageal cancer in the United States. *Cancer*. 2011
15. Ashktorab H, Nouri Z, Nouraie M, et al. Esophageal carcinoma in African Americans: a five-decade experience. *Dig Dis Sci*. 2011; 56(12):3577–3582. [PubMed: 21847566]
16. Enzinger PC, Mayer RJ. Esophageal cancer. *N Engl J Med*. 2003; 349(23):2241–2252. [PubMed: 14657432]
17. Brown LM, Hoover R, Silverman D, et al. Excess incidence of squamous cell esophageal cancer among US Black men: role of social class and other risk factors. *Am J Epidemiol*. 2001; 153(2): 114–122. [PubMed: 11159155]
18. Orringer MB, Marshall B, Chang AC, Lee J, Pickens A, Lau CL. Two thousand transhiatal esophagectomies: changing trends, lessons learned. *Annals of surgery*. 2007; 246(3):363–372. [PubMed: 17717440]
19. Bach PB, Pham HH, Schrag D, Tate RC, Hargraves JL. Primary care physicians who treat blacks and whites. *N Engl J Med*. 2004; 351(6):575–584. [PubMed: 15295050]
20. Breslin TM, Morris AM, Gu N, Wong SL, Finlayson EV, Banerjee M, Birkmeyer JD. Hospital factors and racial disparities in mortality after surgery for breast and colon cancer. *J Clin Oncol*. 2009; 27(24):3945–3950. [PubMed: 19470926]
21. Manfredi C, Kaiser K, Matthews AK, Johnson TP. Are racial differences in patient-physician cancer communication and information explained by background, predisposing, and enabling factors? *J Health Commun*. 2010; 15(3):272–292. [PubMed: 20432108]

Synopsis

Disparities in esophageal cancer outcomes among black and hispanic patients are largely associated with ethnicity/race-related differences in tumor histology, location and the comparative underuse of cancer-directed surgery.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

P-values are based on comparisons between groups with non-hispanic whites as the referent group.

*p<0.05

**p<0.01

Figure 1.

Frequency of surgery by race, tumor location and histology. P-value based on comparisons between groups with non-hispanic whites as the referent group.

*P<0.001

- Mid-Esophagus without Surgery
- Mid-Esophagus with Surgery
- Distal Esophagus without Surgery
- Distal Esophagus with Surgery

Figure 2.
Frequency of surgery by race and tumor location. P-value based on comparisons between groups with non-Hispanic whites as the referent group.

Table 1

Patient and tumor characteristics

Characteristics	All	White	Black	Hispanic	P value
N	6737	5,652 (83.9%)	700 (10.4%)	385 (5.7%)	
Age at diagnosis (years)	66.8	67.2	63.7	66.1	<0.0001
Gender					
Male	5,331 (79.1)	4,525 (80)	492 (70.3)	314 (79.1)	<0.001
Marital Status					
Married	4,214(62.6)	3,724 (65.9)	245 (35.0)	245 (63.6)	<0.001
Stage					
Local	2, 814 (41.8)	2,384 (42.2)	271 (38.7)	159 (41.3)	0.21
Regional	3,923 (58.2)	3,268 (57.8)	429 (61.3)	226 (58.7)	
Histology					
Adenocarcinoma	4,505 (66.9)	4,178 (73.9)	99 (14.1)	228 (59.2)	<0.001
Squamous	2,232 (33.1)	1,474 (26.1)	601 (85.9)	157 (40.8)	
Surgery					
None	3, 576 (53.1)	2, 816 (49.8)	529 (75.6)	231 (60.0)	<0.001
Esophagectomy	2,904 (43.1)	2, 607 (46.1)	156 (22.3)	141 (36.6)	
Local procedure	257 (3.80)	229 (4.10)	15 (2.10)	13 (3.40)	
Location					
Mid-esophagus	1,762 (26.1)	1,210 (21.4)	407 (58.1)	145 (37.7)	<0.001
Distal esophagus	4,975 (73.9)	4,442 (78.6)	293 (41.9)	240 (62.3)	

Analyses performed with Chi-squared test for categorical variables and analysis of variance for continuous variables.

Table 2

Relationship between histology and tumor location

Histology	Tumor Location	
	Distal Esophagus	Mid-Esophagus
Adenocarcinoma	4,107 (91.2%)	398 (8.8%)
Squamous	868 (38.9%)	1,364 (61.1%)

Chi-squared test (p<0.001).

Table 3

Relationship between race and receipt of cancer-directed surgery

Model	Odds Ratio of Surgical Intervention (95% Confidence Interval)	
	Black	Hispanic
Unadjusted	0.33 (0.28–0.40)	0.67 (0.55–0.84)
Adjusted for:		
Patient characteristics [*]	0.30 (0.24–0.37)	0.61 (0.49–0.77)
Patient + tumor characteristics ^{**}	0.48 (0.39–0.60)	0.71 (0.56–0.90)

Analyses performed with logistic regression model for non-hispanic black and hispanic patients compared with non-hispanic white patients.

* Adjusted for patient characteristics (race, age, gender and marital status).

** Adjusted for patient characteristics and tumor characteristics (stage, location and histology).

Table 4

Relationship between race, receipt of cancer-directed therapy and mortality

Model	Hazard Ratio of Mortality (95% Confidence Interval)	
	Black	Hispanic
Unadjusted	1.38 (1.25–1.52)	1.20 (1.05–1.37)
Adjusted for:		
Patient characteristics *	1.38 (1.25–1.53)	1.21 (1.06–1.38)
Patient + tumor characteristics **	1.13 (1.01–1.26)	1.17 (1.03–1.34)
Patient + tumor characteristics + surgery	1.02 (0.91–1.13)	1.08 (0.95–1.24)

Analyses performed with Cox regression model for non-hispanic black and hispanic patients compared with non-hispanic white patients.

* Adjusted for patient characteristics (race, gender and marital status).

** Adjusted for patient characteristics and tumor characteristics (stage, location and histology).