Understanding Racial Disparities in Gastrointestinal Cancer Outcomes: Lack of Surgery Contributes to Lower Survival in African American Patients

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ABSTRACT

Background: Race/ethnicity-related differences in rates of cancer surgery and cancer mortality have been observed for gastrointestinal (GI) cancers. This study aims to estimate the extent to which differences in receipt of surgery explain racial/ethnic disparities in cancer survival.

Methods: The National Cancer Database was used to obtain data for patients diagnosed with stage I–III mid-esophageal, distal esophagus/gastric cardia (DEGC), noncardia gastric, pancreatic, and colorectal cancer in years 2004–2015. Mediation analysis was used to identify variables influencing the relationship between race/ethnicity and mortality, including surgery.

Results: A total of 600,063 patients were included in the study: 3.5% mid-esophageal, 12.4% DEGC, 4.9% noncardia gastric, 17.0% pancreatic, 40.1% colon, and 22.0% rectal cancers. The operative rates for Black patients were low relative to White patients, with absolute differences of 21.0%, 19.9%, 2.3%, 8.3%, 1.6%, and 7.7%. Adjustment for age, stage, and comorbidities revealed even lower odds of receiving surgery for Black patients compared with White patients. The observed HRs for Black patients compared with White patients ranged from 1.01 to 1.42. Mediation analysis showed that receipt of surgery and socioeconomic factors had greatest influence on the survival disparity.

Conclusions: The results of this study indicate that Black patients appear to be undertreated compared with White patients for GI cancers. The disproportionately low operative rates contribute to the known survival disparity between Black and White patients.

Impact: Interventions to reduce barriers to surgery for Black patients should be promoted to reduce disparities in GI cancer outcomes.

See related commentary by Hébert, p. 438

Introduction

Reducing racial disparities in health outcomes in the United States has been recognized as a national priority by the U.S. Agency for Healthcare Research and Quality, among others (1–5). Pronounced disparities in outcomes have been identified for patients with cancer. For example, the American Cancer Society reported in 2017 that the cancer-specific death rate for Black men and women is 24% and 14% higher, respectively, as compared with White men and women. Similar trends hold for gastrointestinal (GI) cancers; there is an association between race and survival (1).

Broad statistical analyses have been previously performed for multiple cancers based on the National Cancer Database (NCDB) or other registries, and significant contributors to survival disparities have included socioeconomic factors and underutilization of treatment, including surgery (6–9). Black patients do not receive surgery as frequently as White patients for multiple cancer and noncancer diagnoses, such as pancreatic cancer (10–13), colorectal cancer (14–17), acute limb ischemia (18–20), and gallstone pancreatitis (21). Because surgical resection is often the most important step in treatment for GI cancer, it is plausible that the measured outcome disparities are partially attributable to failure of our system to deliver surgical care equitably. Differences in underlying perioperative risk including patient medical factors (22), later presentation (23), and higher rates of refusal (24) among minorities are also thought to contribute to the disparity in receipt of surgery and outcomes (25). With so many interconnected factors, it is a conceptual and analytic challenge to measure the impact of each factor, and no study has provided fully adjusted estimates of effects that surgery and other factors have on outcomes in GI cancer.

This study uses the NCDB to fill this gap in the literature and provide a statistical basis for conceptual models of surgical disparities in GI cancers. We measure racial survival disparities in esophageal, gastric, pancreatic, and colorectal cancers with and without adjustment for surgery, stage, patient medical factors, socioeconomic factors, and institutional factors. We then use mediation analysis (or decomposition methods) to estimate the contributions that each of these categories have to the disparity (26). Finally, we evaluate the given reasons that patients did not receive surgery (a variable in the NCDB) in terms of other variables in the model.

Materials and Methods

Data source and variables

Patients were drawn from the NCDB, including years 2004–2014 (27). NCDB is a nationwide, facility-based, comprehensive clinical surveillance resource that captures 70% of newly diagnosed U. S. malignancies. ICD-O-3 diagnosis codes were used to identify patients with cancers of the middle third of the esophagus, distal

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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esophagus/gastric cardia (DEGC), noncardia stomach, pancreas, colon, and rectum. Tumors included were limited to carcinomas.

The variables of critical interest for this study were race/ethnicity, receipt of surgery, and survival. Race and ethnicity were combined such that all people (including those of Black race/ethnicity) listed as ethnically Hispanic were classified as of Latinx race/ethnicity. Other categories were White, Black, Asian/Pacific Islander (API), and other. Surgery was based on the variable "RX_SUMM_PRIM_SITE" and included all resections, regardless of the treatment sequence (whether or not neoadjuvant therapies were given). Survival in months was extracted from the database as well.

Other factors included stage, patient medical factors, socioeconomic factors, and hospital/geographical factors. Patient medical factors were considered separately from stage in the analysis. Patient factors extracted included patient age, sex, Charlson/Deyo Comorbidity score (28) grade, and histology. Histology was divided into squamous versus adenocarcinoma for the esophagus and DEGC; lintitis plastica, signet ring, and diffuse carcinoma versus all other carcinoma of the stomach, and signet ring versus all other carcinoma for the colon and rectum. Socioeconomic factors included ZIP income quartile and insurance. ZIP income quartile is the income quartile for the patient's ZIP code (the main postal code in the United States), among all U.S. ZIP codes. Hospital/geographical factors extracted included region (Northeast, South, Midwest, and West), patient urban context (metro county, adjacent to metro county, rural, or unknown), and cancer center type [community cancer program (CCP), comprehensive CCP, academic center, or integrated network program]. The patient urban context variable is a simplified version of the 9-value item in the NCDB and was classified with hospital factors rather than socioeconomics to focus the latter on financial aspects. Algorithmically created hospital variables included per-organ yearly operative rates and percentiles and per-cancer hospital volume percentiles. The year of diagnosis and reason for not receiving surgery as provided in the NCDB were also extracted.

Analysis

The analysis can be divided into six parts: descriptive statistics, initial Cox regression for survival, generalized linear modeling (GLM) of receipt of surgery, mediation analysis via Cox regression, GLM of reasons for not receiving surgery, and sensitivity analyses. First, descriptive statistics were calculated by organ and by race. Survival and operative rates were compared by organ and race. The primary analysis was limited to nonmetastatic cancer, although metastatic and unknown stage are considered in sensitivity analyses.

Second, Cox regression was conducted to establish the relationship between race/ethnicity and survival with and without multivariable adjustment, and to establish the relationship between receipt of surgery and survival. The proportional hazards assumptions were assessed for the adjusted models.

Third, GLM was used to examine the relationship between race and receipt of surgery with adjustment for stage, patient medical factors, socioeconomic status (SES), and hospital factors. GLM was chosen for easy incorporation of random effects modeling in sensitivity analyses, described below.

Fourth, mediation analysis with Cox proportional hazard modeling was then used to estimate the magnitude of potential mediators' contributions to disparities in survival (26). The "difference of coefficients" method of mediation analysis (29) was used; the magnitude of the contributions was estimated by two methods: the change in HR with (i) the addition of each variable of interest to a model only adjusted by age and year (unadjusted multiple mediation analysis), and (ii) the removal of each variable of interest (or group of variables) from a multivariate model that included all variables (adjusted multiple mediation analysis). The "total effect" is the size of the raw relationship (HR) between race and survival. The "unexplained effect" (also known as "direct effect") is the size of the persistent relationship between race and survival after controlling for all factors in the model. Portions of the "total effect" that are attributable to individual variables are called "specific indirect effects." We assessed interactions among paired groups of variables by removing both from the multivariable model and assessing whether more of the disparity was attributable to both than either individually (30, 31). Factors with minimal impact on unadjusted analysis were left out of the adjusted analysis.

Fifth, an analysis was conducted to characterize the "reason no surgery was performed" variable found in the NCDB. Generalized linear mixed modeling was used for this task. The most common given reasons for nonreceipt of surgery—that surgery was not part of the first course of treatment, that surgery was contraindicated because of patient comorbidities, and that the patient refused surgery—were compared for Black and White patients. The Black/White odds of these responses were compared by race with and without adjustment for age and year; age, year, comorbidities, histology, and stage; and all variables.

Finally, three sensitivity analyses were performed to see whether changes in variables or inclusions affected the relationship between receipt of surgery and the disparity. First, the receipt of surgery variable was replaced with one that reflected receipt of surgery and whether diagnosis and surgery took place on the same day (a marker for an emergent operation). Second, the mediation analysis was reperformed in stage IV and unknown clinical stage cohorts. Finally, the mediation analysis was reperformed in the stage I–III cohort using random effects modeling by hospital ID to adjust for potential clustering by hospital.

Results

A total of 600,063 patients with stage I–III cancer diagnoses were included in the study: 3.5% mid-esophageal, 12.4% DEGC, 4.9% noncardia gastric, 17.0% pancreatic, 40.1% colon, and 22.0% rectal cancers (**Table 1**). Type of surgery was examined, but not included in the final model as it was not a significant predictor. An additional 323,106 stage IV patients were included in the sensitivity analyses. Including all primary sites of cancer, the cohort studied was 79.4% White, 10.7% Black, 5.2% Latinx, 3.1% (API), and 1.6% other. Black and Latinx patients were more likely to be from poorer areas and be younger than other patients. Black patients were more likely to have squamous histology (per-cancer details are given in the Supplementary Tables S1 and S2).

Race/ethnicity, survival, and receipt of surgery

Strong relationships between (i) race and survival, (ii) receipt of surgery and survival, and (iii) race and receipt of surgery were observed and are shown in **Fig. 1**. Unadjusted 1-year and 5-year survival differences between Black and White patients were seen in esophageal cancer (1 year: 50% vs. 61%) and DEGC (1 year: 71% vs. 60%). Substantial differences were also observed between patients who did and did not receive surgery (such as colon 1-year: 88% vs. 41%). Differences in unadjusted operative rates were most pronounced between Black and White patients for the proximal cancers (esophageal cancer: 38% vs. 17%; Supplementary Fig. S1). With only age adjustment, significant survival differences were identified for most cancers (**Fig 1**, precise values given in Supplementary Table S3). Black patients had the lowest survival relative to White patients [HR and 95%

Table 1. Descriptive statistics.

	Race/ethnicity					
	White	**Black**	**Latinx**	**API**	**Other**	***N***
White	100.0					476,721
Black		100.0				64,228
Latinx			100.0			31,005
API				100.0		18,325
Other					100.0	9,784
Mid-esophagus	3.3	5.6	2.5	3.4	3.5	20,852
DEGC	14.0	5.1	7.4	6.1	12.0	74,427
Stomach	3.4	9.0	12.6	17.4	6.7	29,583
Pancreas	17.0	18.4	15.4	14.9	18.2	102,225
Colon	40.0	44.6	38.2	34.5	35.9	240,832
Rectum	22.4	17.3	23.9	23.8	23.7	132,144
<55	17.7	24.9	29.4	24.6	24.4	116,526
55–64	23.3	28.5	25.7	25.1	26.2	144,307
65–74	27.5	25.4	24.6	25.7	26.0	162,339
75+	31.5	21.2	20.3	24.6	23.4	176,891
Stage I	40.6	40.7	37.2	40.7	41.1	242,494
Stage II	32.7	31.5	32.8	31.2	32.1	195,328
Stage III	26.7	27.8	30.0	28.1	26.9	162,241
Adenocarcinoma	95.9	90.1	92.5	89.4	93.8	569,245
Esophagus: squamous carcinoma; gastric: lintitis plastica/diffuse, colorectal: signet cell	4.1	10.0	7.5	10.6	6.2	30,818
No radiation	65.7	70.9	68.6	68.0	68.4	399,166
Radiation given	33.6	28.2	30.4	30.9	30.1	196,267
Unknown	0.7	0.9	1.0	1.1	1.5	4,630
No chemotherapy	48.8	49.5	44.2	46.2	49.1	291,325
Chemotherapy given	48.5	46.9	51.8	49.9	45.3	290,861
Unknown	2.7	3.6	4.0	4.0	5.6	17,877
Grade 1	8.8	8.8	8.4	8.0	7.7	52,317
Grade 2	46.9	46.3	45.6	46.2	43.5	280,361
Grade 3	20.1	18.1	22.4	23.2	20.8	120,430
Grade 4	1.4	0.9	1.3	1.3	1.4	7,852
Unknown	22.9	26.0	22.4	21.2	26.6	139,103
Surgery given	75.7	70.0	74.8	76.9	72.7	450,008
Surgery day of diagnosis	20.2	21.9	19.2	18.7	21.4	121,684
Male sex	57.3	50.4	57.0	55.0	58.4	339,031
No comorbidities	70.7	67.5	71.4	76.0	74.8	423,888
1 Comorbidity	21.2	23.3	21.6	18.8	18.9	128,114
2 Comorbidities	5.8	6.2	4.8	3.6	4.4	33,962
3 Comorbidities	2.3	3.0	2.3	1.6	1.8	14,099
Operative rate 0%–25th %ile	23.4	30.5	35.7	24.3	27.6	149,530
25%–75%ile	50.4	47.5	44.6	52.0	43.8	298,593
75%–90%ile	15.8	14.3	11.2	14.4	16.1	92,342
90+%ile	10.3	7.7	8.5	9.4	12.5	59,598
Community cancer program (CCP)	10.9	8.0	7.8	10.9	7.5	62,204
Comprehensive CCP	43.3	33.6	35.4	33.7	27.8	248,070
Academic program	34.1	43.9	39.7	44.8	50.4	216,414
Integrated network cancer program	10.0	12.0	12.0	7.3	11.2	61,307
Other	1.7	2.5	5.0	3.4	3.1	12,068
Hospital volume 0%–25th %ile	25.6	21.9	21.9	22.4	18.0	148,734
25%–75%ile	49.8	52.2	51.4	48.5	46.1	300,490
75%–90%ile	14.6	15.4	14.8	18.3	22.6	89,801
90+%ile	9.9	10.4	11.9	10.9	13.4	61,038
2004–2007	22.5	20.9	19.4	19.9	23.9	132,619
2008–2011	37.6	38.0	36.7	34.6	36.9	225,024
2012–2015	39.9	41.1	43.9	45.5	39.2	242,420
Northeast	22.9	17.7	20.1	21.0	24.2	132,995
Midwest	27.6	20.9	8.7	11.4	23.0	152,153
South	33.7	54.1	36.5	15.9	27.4	212,081
West	14.1	4.8	29.7	48.4	22.3	90,766
Unknown	1.7	2.5	5.0	3.4	3.1	12,068

(Continued on the following page)

Table 1. Descriptive statistics. (Cont'd)

	Race/ethnicity					
	White	Black	Latinx	API	Other	N
Zip income quartile: bottom	13.9	43.6	26.3	7.2	17.8	105,616
Second	24.0	22.3	24.0	14.3	20.5	140,844
Third	27.8	18.3	26.8	25.8	26.0	159,608
Top quartile	33.3	14.9	22.2	51.8	34.5	188,102
Unknown	1.0	0.9	0.8	0.9	1.2	5,893
No insurance	2.1	5.8	9.6	4.6	3.2	17,743
Private insurance	34.8	32.2	33.7	40.1	37.8	208,121
Medicaid	3.5	10.9	14.1	11.7	6.8	31,050
Medicare	56.4	47.4	38.5	41.0	42.1	322,945
Other government	1.2	1.3	0.7	0.9	4.1	7,275
Unknown	2.0	2.4	3.4	1.7	6.0	12,929
Urban county	79.0	88.6	92.7	94.8	79.0	487,498
Adjacent to urban county	12.2	7.5	3.4	1.2	10.4	65,399
Rural county	5.6	1.8	1.7	1.2	7.4	29,279
Unknown	3.1	2.2	2.2	2.8	3.3	17,887

confidence interval (CI) for cancers of the mid-esophagus 1.42, 1.36–1.48; DEGC 1.37, 1.31–1.43; stomach 1.01, 0.97–1.05; pancreas 1.12, 1.10–1.15; colon 1.22 1.19–1.25; rectum 1.36, 1.31–1.40]. API patients had the highest survival compared with White patients.

Receipt of surgery was among the strongest adjusted predictors of survival, with HRs ranging from 2.25 (95% CI, 2.15–2.35) for mid-esophageal cancer to 4.06 (95% CI, 3.95–4.18) for colon cancer. Multivariable adjustment accounts for much of the Black-White survival disparity, although the disparities are not completely accounted for in colorectal cancer.

The observed Black-White difference in receipt of surgery persists on multivariable adjustment via GLM with adjusted ORs of 0.87 (050–0.64) for esophagus, 0.53 (0.48–0.57) for DEGC, 0.79 (0.74–0.86) for stomach, 0.64 (0.60–0.68) for pancreas, 0.78 (0.73–0.83) for colon, and 0.71 (0.70–0.88) for rectum cancers.

Mediation analysis

Figures 2 and **3** quantify the effect of variables on disparate outcomes observed in Black compared with Whites patients (all numeric effect values are given in the Supplementary Table S4). Unadjusted specific indirect effects comparing API and Latinx patients to White patients are displayed in Supplementary Figs. S2 and S3. On assessment of the proportional hazards assumptions, we found that some variables had variation in the HR over time, but that none crossed 1.0. Further assessment of the meaning of this result is described below under the heading "additional analyses." Receipt of surgery is the strongest single mediator of the difference between Black and White patients in survival for all GI cancers except colon [unadjusted specific indirect effects (ΔHRs) for mid-esophagus: 0.27, DEGC: 0.25, stomach: 0.08, pancreas: 0.13, colon: 0.06, and rectum: 0.12]. The proportions of the survival disparity attributable to lower operative rates in Black patients for mid-esophagus, DEGC, pancreas, colon, and rectum cancer were 64%, 67%, 100%, 25%, and 32%, respectively, prior to adjustment for other factors. Stage at presentation was also a contributor to the disparity for proximal cancers. **Figure 2** is abridged in that factors that had a minimal impact on the disparity are excluded; facility type, region, urban/rural context, chemotherapy, radiation, grade, and sex are left out. All specific indirect effects are given in Supplementary Table S4.

Figure 3 depicts the adjusted specific indirect effects of the individual variables on the HR. For Black patients, receipt of surgery was again the strongest mediator of the survival disparity for gastric, pancreatic and rectal cancer (adjusted specific indirect effects or ΔHRs: 0.06 for mid-esophagus, 0.09 for DEGC 0.07 for gastric, 0.06 for pancreas, 0.03 for colon, and 0.06 for rectum). Receipt of surgery and ZIP income quartile were among the most important mediators for all cancers; the adjusted proportion of disadvantage attributable to surgery and SES ranged from 14% to 48% and 16% to 34%, excluding gastric cancer. For gastric cancer, although Black patients have no disadvantage in overall outcomes, they do appear to have a disadvantage in receipt of surgery that is associated with higher mortality than they could experience otherwise, compared to White patients. Histology contributed to the disparity substantially in esophageal and DEGC cancers, but Black patients had advantageous histology compared with White patients in gastric cancer. There were substantial interactions and overlaps among the variables, especially for esophageal and DEGC cancer; more than half of the disparity could be attributed to two or more factors for these segments. In contrast to Black patients, Latinx and Asian patients were observed to have survival advantages for all cancer types compared to White patients. Latinx patients appear to be disadvantaged by most of the measured variables in the model, but experience survival advantages nonetheless. The API population was not consistently disadvantaged by any factor in the model.

Analysis of given reason for nonoperative management

Table 2 shows the percent of patients who received surgery and the reasons listed for patients not having received surgery. Black patients were more likely to be classified as having refused surgery, having medical contraindications to surgery, or as surgery not being the first course of their treatment. Adjustment for the factors that should underlie these classifications—age, stage, and comorbidities—revealed an even larger disparity between Black and White patients for many cancers. Controlling for all factors in the multivariable logistic model similarly identified disproportionate, unexplained likelihood that Black patients would be classified as not receiving surgery for the above reasons (**Table 2**).

Additional analyses

Sensitivity analyses for use of random effects modeling to manage potential clustering among hospitals and controlling for receipt of surgery on the same day as diagnosis did not alter the contributions of

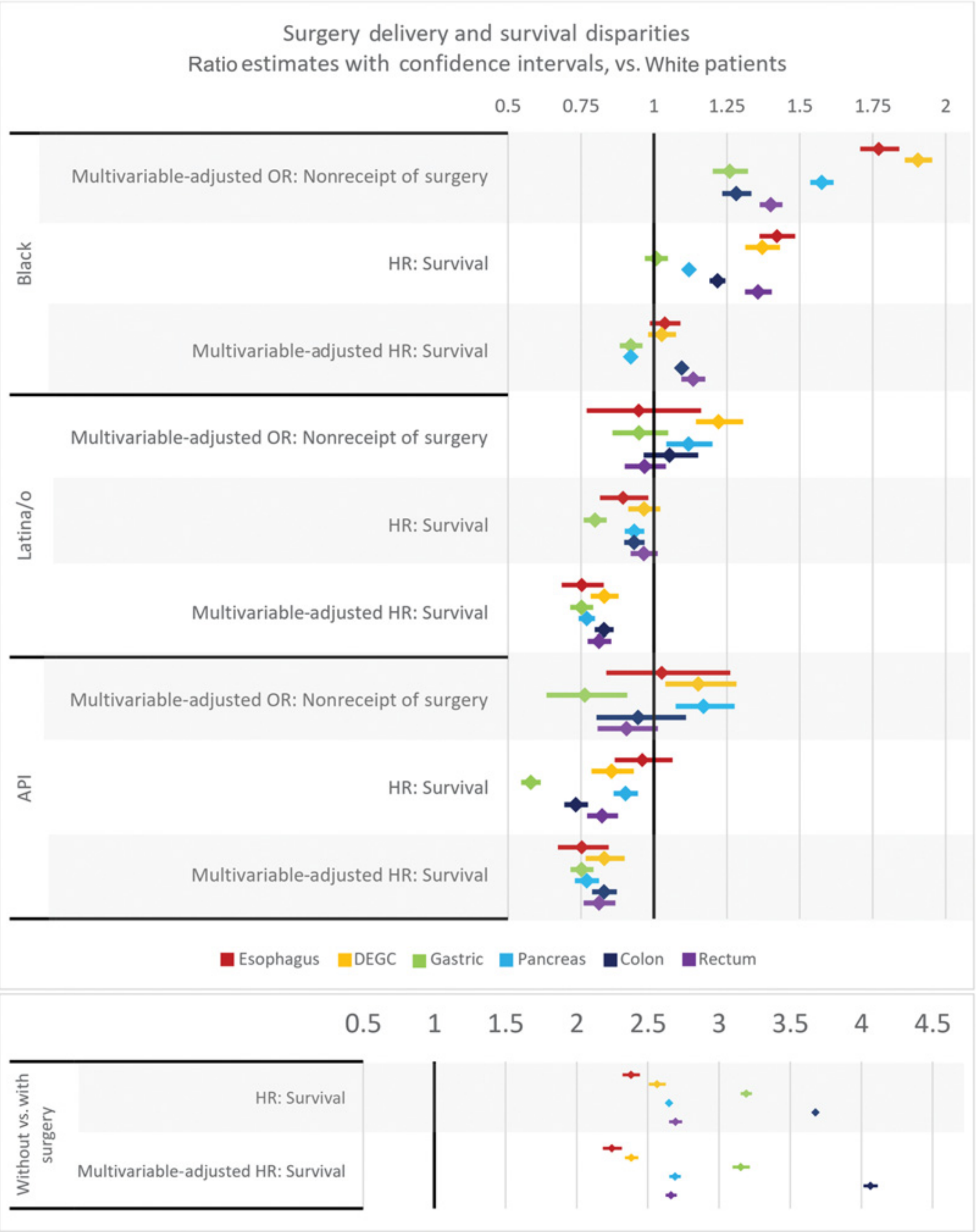

Figure 1.
Surgery delivery and survival disparities: ratio estimates with CIs, versus White patients.

differences in receipt of surgery to outcome disparities (Supplementary Table S5). For stage IV esophagus, gastric, and pancreatic cancer, there is no contribution of receipt of surgery to a survival disparity. To better assess the proportional hazards assumptions over time, the mediation analysis was repeated with GLM for survival to years 1, 2, 3, and 5. The specific indirect effects of surgery on survival were measured at each of these intervals. For the upper GI cancers, surgery had a larger contribution to the disparity in later years than at year 1, while for colorectal cancer the contribution of surgery to disparities diminished over time (**Fig. 4**).

Discussion

This study found that in all cancers evaluated except gastric cancer, a difference in receipt of surgery contributes a substantial proportion of the survival disparity observed for Black patients compared with White patients. For mid-esophageal and proximal gastric cancer, more than half of the disparity can be attributed to gaps in delivery of surgery. Another significant contributor was SES as measured by ZIP income quartile and insurance. Histology and stage had a substantial impact for the proximal GI cancers, but not others. Numerous other factors—

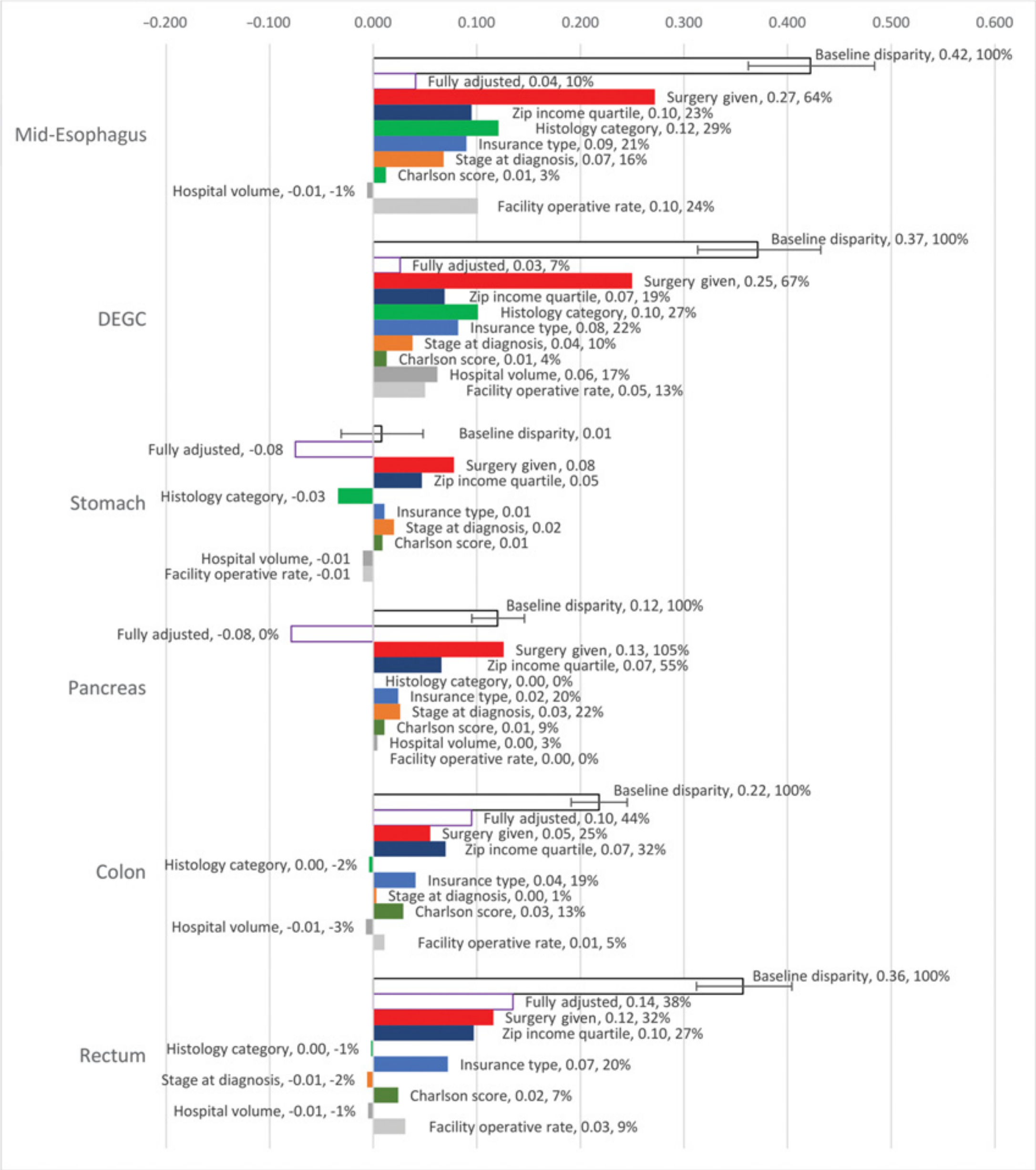

Figure 2.

Unadjusted mediation analysis: Black versus White patients. Effects of selected variables on survival disparity, reported as change in HR with addition of variable to model and percent of baseline disparity (total effect) explained. Direct effect labeled as "fully adjusted." All other values are specific indirect effects.

urban/rural geography, hospital factors, and patient comorbidities—had relatively little influence.

Other studies have emphasized the roles of patient, social and hospital factors in mediating the relationship between race and survival. One recent study used a mediation analysis to evaluate contributors to disparities for multiple cancers in a California-based registry and identified stage at presentation as a leading factor, although their methodology did not include adjustment of stage's contributions for any other factor (9). Differences in SES (7, 32) and insurance among racial groups (33, 34) have been found to explain the disparities in part. Other factors, particularly age, bias raw mortality rates from cancer in favor of minorities, because the median age of the U.S. Black population is 34, compared with 40 for the White population (35). Furthermore, discrimination, itself, can lead to worse cancer outcomes through biological mechanisms, such as stress-induced immunosuppression (36, 37). Our findings are consistent with these patterns, but additionally we found that receipt of surgery is a prominent mediator of the disparity after adjustment for these factors.

Included in our findings is a robust evaluation of interactions among paired groups of variables. In our case, this method clarified considerable overlap among variables. For example, in the esophageal cancers, patient factors of histology and comorbidities appear to influence the disparity in part through influencing surgical decisions

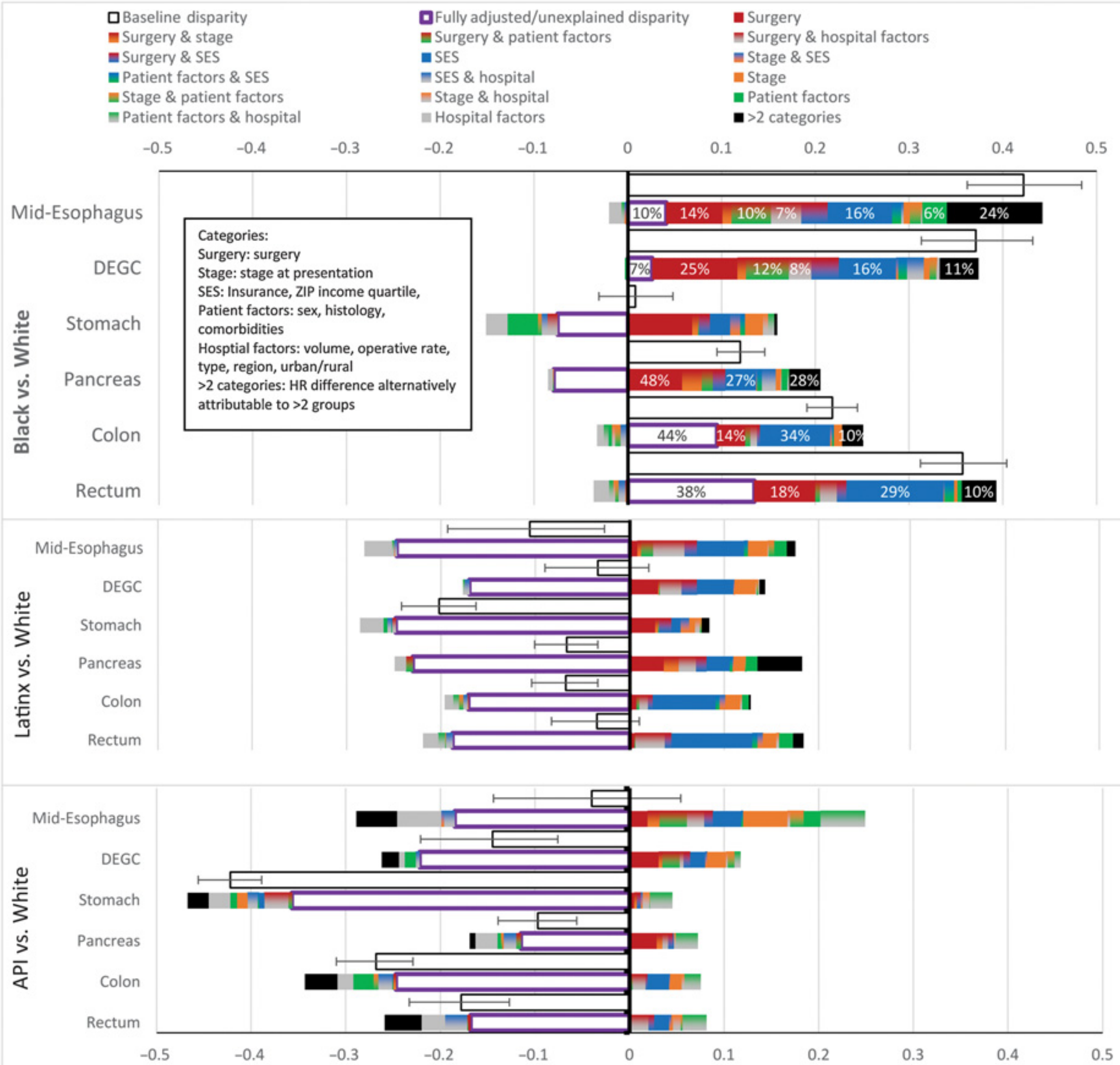

Figure 3.

Adjusted mediation analysis: effects of grouped variables on disparity after mutual adjustment. Total effects (black outline), direct effects (purple outline), and individual contributions of variable groups are displayed. Paired contributions are also displayed (when effect could be attributed to either of two variable groups, but no other). Data labels correspond to the percent of the total effect attributable to the specific indirect effect. API, Asians/Pacific Islanders. DEGC, distal esophagus/gastric cardia.

(because we do not expect surgical decisions to influence these baseline patient factors).

As a target for intervention, receipt of surgery may be a practical option to address cancer outcomes disparities, compared with addressing pervasive differences in SES. To improve access to surgery, some authors have recommended expansion of access via public insurance, intensified use of explicit treatment algorithms, alignment of hospital incentives with elimination of disparities, and improving patient-centered tools for navigation of health and hospital systems (38). In particular, governmental interventions directed at extending insurance coverage (such as state-level expansions of Medicaid vs. states that had not at the time) have been associated with measurable decreases in cancer disparities over time (39, 40). Statewide efforts to ensure that Black patients, specifically, receive surgery (41) have also led to measurable reductions in survival disparities. One example of an algorithm apparently affecting a disparity is that addition of MELD scoring to a liver transplantation algorithm resulted in elimination of a pre-MELD racial disparity in both receipt of transplant and survival (42).

A part of the Black/White disparity in receipt of surgery is also attributable to disproportionate rates of "refusal." As has been recognized previously for lung (43) and colorectal cancer (44), Black patients are more likely to be recorded as refusing surgery. However, the underlying cause of this difference is not well understood. We cannot simply assume that Black patients' deeply held values would justify a disproportionate rate of refusal of life-saving surgery; to do so would be to arbitrarily dismiss, without investigation, the likely roles of discrimination and systemic racism. Deficiencies in the medical

Table 2. Reasons for nonoperative management.

	Surgery receipt/given reason for not receiving surgery	Given reasons for no surgery by race: White %	Black %	Latinx %	API %	Other %	Adjusted logistic models, Black vs. White OR: Unadjusted OR	+Age and year aOR	+Charlson, histology and stage aOR	All variables aOR
Mid-esophagus	Received surgery	38%	17%	30%	27%	34%	**0.33**	0.27	**0.41**	0.57
	Surgery not first course	50%	68%	57%	57%	53%	**1.19**	1.37	**1.16**	1.16
	Too sick for surgery	7%	8%	6%	9%	3%	**2.18**	2.46	**1.79**	1.33
	Refused	2%	3%	1%	3%	3%	**1.34**	1.54	**1.46**	1.43
DEGC	Received surgery	57%	38%	52%	52%	60%	**0.45**	0.35	**0.45**	0.52
	Surgery not first course	31%	49%	36%	35%	27%	**1.21**	1.42	**1.25**	1.17
	Too sick for surgery	5%	7%	5%	6%	5%	**2.13**	2.59	**2.01**	1.63
	Refused	2%	3%	2%	3%	2%	**1.50**	1.77	**1.77**	1.70
Stomach	Received surgery	68%	66%	71%	79%	68%	**0.90**	0.77	**0.77**	0.80
	Surgery not first course	22%	23%	21%	15%	21%	**1.06**	1.25	**1.21**	1.22
	Too sick for surgery	5%	5%	3%	2%	2%	**1.05**	1.17	**1.18**	1.11
	Refused	2%	3%	1%	2%	2%	**1.44**	1.94	**1.92**	1.89
Pancreas	Received surgery	39%	30%	36%	36%	35%	**0.69**	0.59	**0.59**	0.63
	Surgery not first course	48%	54%	52%	52%	50%	**1.26**	1.35	**1.29**	1.25
	Too sick for surgery	9%	11%	7%	8%	7%	**1.29**	1.42	**1.38**	1.21
	Refused	2%	2%	1%	2%	2%	**0.99**	1.24	**1.29**	1.12
Colon	Received surgery	96%	94%	95%	96%	95%	**0.70**	0.55	**0.55**	0.79
	Surgery not first course	2%	3%	3%	2%	4%	**1.23**	1.76	**1.71**	1.25
	Too sick for surgery	1%	1%	1%	1%	1%	**1.41**	1.64	**1.65**	1.13
	Refused	1%	1%	0%	0%	0%	**1.59**	2.66	**2.60**	1.89
Rectum	Received surgery	85%	77%	80%	85%	81%	**0.60**	0.54	**0.54**	0.72
	Surgery not first course	10%	14%	13%	9%	12%	**1.50**	1.85	**1.81**	1.60
	Too sick for surgery	1%	2%	1%	1%	1%	**1.55**	1.67	**1.68**	1.19
	Refused	2%	3%	1%	2%	2%	**1.83**	2.15	**2.15**	2.00

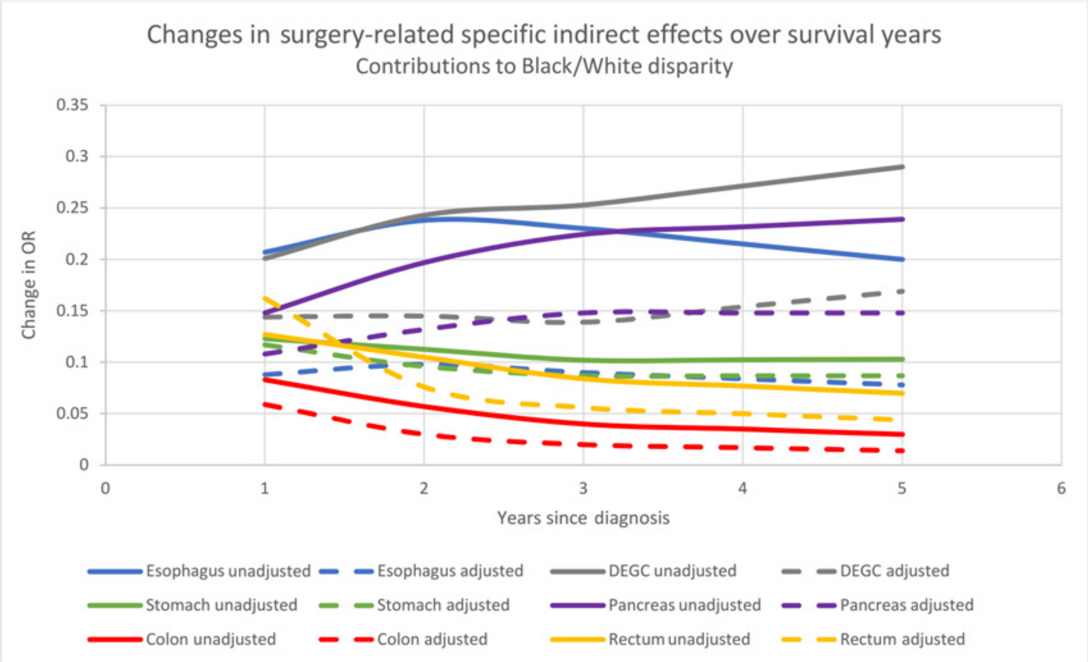

Figure 4.

Contribution of receipt of surgery to Black/White disparity over time: mediation analysis based on generalized linear regression for 1-, 2-, 3-, and 5-year survival. The degree of mediation does change over time but not in a way that would affect our primary finding.

community's ability to establish patient-physician trust (given previous and ongoing, valid reasons for patient distrust; ref. 45) or physician cultural competency may also be considered as possibly contributing to refusal (46). Numerous interventions have been developed to improve mutual understanding among patients and physicians, but effects on outcomes have not yet been thoroughly studied (47).

Although we have found that the gap in receipt of surgery contributes to mortality differences, we also observed that part of the gap in receipt of surgery between minority and White patients remains unexplained. This study anticipates and rules out many commonly offered explanations for the Black/White differences. In particular, to the extent that patient medical factors are captured by stage, histology, and comorbidities and sex, medical factors cannot explain the disparate delivery of surgical care. However, we do not provide a positive identification of the cause of the disparate rates of surgery, so we are left to speculate about variables not included in the NCDB, such as frailty or social support.

Setting aside the differences in operative rates, the unexplained disparities in outcomes are even more pronounced between White patients and Asian/Pacific Islander or Latinx patients. Possible contributors include the so-called healthy immigrant effect, which is a complex conglomeration of differences in SES, selective immigration, and possibly genetic, cultural or environmental factors (48). Although ancestry-related genetic differences are increasingly recognized in breast (49, 50) and prostate (51) tumors, genetic ancestry and the social construction of race are often scientifically incongruous categorizations. The fact that subpopulations within the colloquial racial groups can have distinct genetic risk profiles emphasizes that variation within groups can be even more scientifically significant than variation among people of different skin colors (52). However, given the field's historical missteps into racist pseudoscience (53–55), claims of genetic differences among racial/ethnic groups should be held to the highest level of scientific rigor, or even replaced with more scientifically valid groupings (56).

Ultimately, to clarify the underlying causes of disparities due to differences in receipt of surgery, an institution-level study is needed where patients and physicians can be interviewed. Alternatively, interventions could be planned where physicians and practice groups are monitored and then informed of their disparate operative rates, and given the opportunity to reflect on, explain and correct them. In this way, the treatment-related disparity can be handled in the via the same interventional strategies as we use to handle other measure of quality. Previous attempts to improve the quality of care received by minority patients have improved adherence to the standard of care for all patients (41), and some studies have shown that *treatment* disparities disappear in an equal-access system (i.e., the military; ref. 57).

This study has limitations. The NCDB data on the SES of patients is limited to ZIP code–level income quartile, which lacks the specificity of more granular measures such as census-block level factors. Adjustment for more detailed measures of socioeconomic factors and psychosocial stressors could have an effect on our findings. The NCDB captures the majority of cancer diagnoses in the United States, but those it does not capture are less likely to be urban academic centers, and this fact could bias our findings. We did not obtain enough statistical power to perform meaningful analyses on disparities affecting Native Americans. The proportional hazards assumption limits the precision of our model as a predictor of patient-level outcomes over time. On this point, we postulate that the best approach in the future will involve artificial intelligence-assisted model development. Because this is a database study, we were unable to verify the reasons for nonoperative management via chart review or interviews. We did not perform significance testing or construct CIs for the changes in HRs because our aim was primarily to obtain a qualitative grasp of receipt of surgery's influence on racial disparities in survival.

Conclusion

Cancer mortality disparities between Black and White patients from esophageal, pancreatic, colon, and rectum cancer are partially attributable to differences in operative rates. The differences in operative rates are not explained by hospital factors, stage at presentation, comorbidities, or any other factor available in the NCDB. Further studies are needed to identify the underlying causes of these differences in rates of surgery and to develop and administer interventions to correct them.

Authors' Disclosures

K.T. Papalezova reports personal fees from COTA outside the submitted work. No disclosures were reported by the other authors.

Authors' Contributions

J.N. Bliton: Conceptualization, formal analysis, investigation, visualization, methodology, writing–original draft, writing–review and editing. **M. Parides:** Formal analysis, writing–review and editing. **P. Muscarella:** Writing–review and editing. **K.T. Papalezova:** Writing–review and editing. **H. In:** Conceptualization, resources, data curation, software, formal analysis, supervision, funding acquisition, validation, writing–review and editing.

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