

Postsurgical Disparity in Survival between African Americans and Caucasians with Colonic Adenocarcinoma

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Supported in part by grants from the National Cancer Institute (R01-CA98932-01 and R03-CA097542-01), which are funded by the National Institutes of Health.

The authors thank Sameera Vohra, M.D., for her assistance in preparing the current article.

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Received September 5, 2003; revision received April 5, 2004; accepted April 9, 2004.

BACKGROUND. Studies of colorectal adenocarcinoma (CRC) indicate a higher mortality rate for African Americans compared with Caucasians in the United States. In the current study, the authors evaluated the racial differences in survival based on tumor location and pathologic stage between African-American patients and Caucasian patients who underwent surgery alone for CRC.

METHODS. All 199 African American patients and 292 randomly selected, non-Hispanic Caucasian patients who underwent surgery between 1981 and 1993 for first primary sporadic CRC at the University of Alabama–Birmingham (Birmingham, AL) or an affiliated Veterans Affairs hospital were assessed for differences in survival. None of these patients received preoperative or postoperative neoadjuvant or adjuvant therapy. Survival curves were generated using the Kaplan–Meier method, and hazard ratios with 95% confidence intervals (95% CI) were estimated from Cox proportional hazards models, adjusting for demographic and tumor characteristics.

RESULTS. African Americans were 1.67 (95% CI, 1.21–2.33) and 1.52 (95% CI, 1.12–2.07) times more likely to die of colonic adenocarcinoma (CAC) within 5 years and 10 years of surgery, respectively, compared with Caucasians. Racial differences in survival were observed among patients with Stage II, III, and IV CAC; however, the strongest and statistically significant association was observed among patients with Stage II CAC. There were no significant racial differences in survival in patients with rectal adenocarcinomas.

CONCLUSIONS. The current findings suggest that the decreased overall survival at 5 years and 10 years postsurgery observed in African-American patients with CAC may not be attributable to tumor stage at diagnosis or treatment but may be due to differences in other biologic or genetic characteristics between African-American patients and Caucasian patients. *Cancer* 2004;101:66–76.

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KEYWORDS: colon adenocarcinoma, African Americans, survival disparity, tumor stage, tumor site.

Colorectal carcinoma (CRC) is the third most common malignancy and the second most common cause of cancer mortality among men and women in the United States. In 2003, there were an estimated 147,500 new cases of CRC and 57,100 deaths due to this malignancy.¹ In the United States, there are racial differences in CRC incidence, mortality, and survival. Compared with Caucasians, African Americans have higher incidence and mortality rates and lower survival rates.² Recent trends indicate that the incidence of CRC among Caucasians has declined slightly and recently stabilized, whereas CRC incidence among African Americans has increased. The

racial discrepancy is even more prominent with respect to mortality: Mortality rates have declined steadily for Caucasians, whereas they have increased for African Americans, and particularly African-American men. For each disease stage at diagnosis, 5-year relative survival rates are lower for African Americans with CRC than for Caucasians.²

Several studies of survival differences between African-American and Caucasian patients with CRC have reported poorer prognosis and shorter survival among the former group³⁻¹⁵ (Table 1). These studies analyzed survival and/or mortality among patients with colonic, rectal, or colorectal carcinoma (patients with colonic and rectal tumors were analyzed as a single group). A variety of explanations for the racial disparity in survival have been proposed, including differences in age, advanced disease stage at the time of diagnosis, treatment options, socioeconomic factors, and biologic characteristics (Table 1).

We conducted survival analyses to elucidate the differences in survival between African-American patients and Caucasian patients with CRC based on tumor site and tumor stage, because neoplasia of the colon and the rectum should be viewed as distinct disease entities, each with their own prognostic factors. All patients underwent surgery (alone) with curative or palliative intent at the University of Alabama-Birmingham (UAB; Birmingham, AL) or at an affiliated Birmingham Veterans Affairs (VA) hospital. The current clinical cohort of patients may represent the population dynamics of the southeastern United States.

MATERIALS AND METHODS

We identified 819 patients from the UAB and VA tumor registries who had undergone surgery from 1981 through 1993 for colorectal adenocarcinoma. From this group, we included all African-American patients ($n = 199$) and 300 randomly selected non-Hispanic Caucasian patients who were diagnosed with first primary CRCs with or without distant metastases in the study. Information related to patient demographics and clinicopathologic characteristics were extracted from medical records and pathology reports, respectively. We reviewed charts and surgical pathology reports to ensure correct staging and other clinical information. During our initial selection process, patients who had multiple primary tumors within the colon/rectum, multiple malignancies, or a family or personal history of malignancy were excluded from the study population; therefore, the study cohort consisted of only those patients who had sporadic first primary CRCs. Because we were interested in determining racial differences in survival by anatomic subsite, patients with unspecified tumor location were not

included in this study. To control for treatment bias between African-American and Caucasian patients, we included patients who underwent surgery as their only therapeutic intervention and excluded patients who received presurgical or postsurgical chemotherapy. Patients who died within 1 week of their surgery were excluded from the analyses ($n = 8$). The final cohort ($n = 491$) for the current analyses included of 199 African-American patients and 292 Caucasian patients. These racially distinct patients are under the care of a uniform group of physicians and health care workers.

We used the UAB and VA tumor registries to obtain follow-up information related to patient vital status. Patients were followed by the UAB or VA tumor registries until death or until the date of their last documented contact within the study time frame. The tumor registries ascertain outcome (mortality) information directly from patients (or living relatives) and their physicians through telephone and mail contacts. This information is validated further by state death lists. The tumor registries update follow-up information every 6 months, and follow-up of the current cohort ended on May 30, 2003, one month before the current analyses were performed.

Death due to either colonic carcinoma or rectal carcinoma was the outcome (event) of interest in this study. The number of months from the date of surgery to death or the date of last contact was used to measure the time at risk. Patients who died of a cause other than CRC or who were alive at the time of last follow-up were censored in the current analyses.

Tumor variables included Stages I, II, III, and IV according to the International Union Against Cancer staging system; tumor grade (degree of differentiation); and anatomic tumor location. Pathologic tumor staging was performed according to the criteria of the American Joint Committee on Cancer.¹⁶ Histologic grade was coded as *poorly differentiated*, *moderately differentiated*, or *well differentiated*.¹⁷ International Classification of Diseases for Oncology codes were used to specify anatomic tumor locations.¹⁸ Anatomic subsites were grouped into the *proximal colon* (cecum, ascending colon, and first two-thirds of the transverse colon), the *distal colon* (the last one-third of the transverse colon, splenic flexure, descending colon, and sigmoid colon), and the *rectum*.

Statistical Analysis

We used the chi-square test to evaluate differences in baseline characteristics between African-American patients and Caucasian patients. Kaplan-Meier survival curves stratified by race were estimated, and the significance of differences between groups was com-

TABLE 1
Review of Studies Evaluating Differences in Survival between African Americans and Caucasians with Colorectal Adenocarcinoma

Study (yr)	Location of study population	No. of patients in study population	% AA patients	Yrs diagnosed	Source of patient data	Descriptive study notes	HR (95% CI) ^a	Variables included in multivariate analysis ^b	Other statistically significant variables in multivariate analysis of survival
Colon carcinoma									
Current study	Alabama	398 (colon carcinoma)	42	1981–1993	University hospital and VA Medical Center	Evaluated racial differences in survival based on tumor site and disease stage in AA and Caucasian patients who underwent surgery for first primary CAC	5 yr: 1.67 (1.21–2.33); 10 yr: 1.52 (1.2–2.07)	Age, gender, hospital, stage, grade, anatomic subsite	Increasing age (10 yr survival only), disease stage, tumor grade (poor differentiation)
Dignam et al. (1999) ¹⁵	U.S., Canada	5969 (all trials combined)	10	1977–1994	NSABP	Combined survival analysis was performed for five clinical trials of the NSABP	1.21 (1.06–1.37) (5 combined trials)	Age, gender, no. of positive lymph nodes, tumor location, treatment	Increasing age, male gender, increasing stage, single tumor location vs. multiple locations
Mayberry et al. (1995) ⁹	Atlanta, GA; New Orleans, LA; SF/Oakland, CA	975	46	1985–1987	Population-based cancer registries	Authors suggest that the racial differences in survival were confined to Stage II/III disease.	1.30 (1.00–1.80)	Age, gender, location, stage, grade, site, symptoms, comorbidities, health behavior, treatment, sociodemographics	Multivariate analysis of other prognostic factors not reported
Dayal et al. (1987) ⁵	U.S. (Comprehensive Cancer Centers)	3617	30	1977–1982	CCPDS	Examined the independent effects of race and SES on survival of patients with CRC	1.28 ($P < 0.001$) ^c	Age, SES, gender, stage	Increasing age
Rectal carcinoma									
Current study	Alabama	93 (rectal carcinoma)	32	1981–1993	University hospital and VA Medical Center	Evaluated racial differences in survival based on tumor site and stage in AA and Caucasian patients who underwent surgery for first primary rectal tumors	5 yr: 0.69 (0.29–1.62); 10 yr: 0.73 (0.31–1.72)	Age, gender, hospital, stage, grade	Tumor stage

Dignam et al. (2003) ¹³	U.S. and Canada	512 (Protocol R-01), 662 (Protocol R-02), 1174, (combined)	11, 7, 9	1977–1992	NSABP	An NCI-sponsored clinical trials group; two clinical trial protocols were evaluated along with a combined analysis	Combined: 1.45 (1.09–1.93)	Age, gender, no. of positive lymph nodes, tumor location, surgery type, treatment	Increasing age, tumor stage, surgery type
Dayal et al. (1987) ⁵	U.S. (Comprehensive Cancer Centers)	1528	23	1977–1982	CCPDS	Study examined the independent effects of race and SES on survival of patients with carcinoma of the colon and rectum	1.44 ($P < 0.001$) ^c	Age, SES, gender, stage	Increasing age, male gender
Michelessi et al. (1988) ¹⁴	Chicago, IL	147	33	1965–1981	University medical center	Patients with rectal tumors who underwent surgery; only patients with Duke stage B and C tumors were included in multivariate analysis.	1.75 ($P < 0.03$) ^d	Duke stages B and C, tumor morphology, vascular-lymphatic microinvasion	Duke stage (B vs. C), tumor morphology, vascular-lymphatic microinvasion
CRC (combined analysis of colon and rectal carcinoma)									
Govindarajan et al. (2002) ⁷	Arkansas	617	31	1984–1997	University hospital	Differences in survival persisted after the inclusion of SES factor	1.5 (1.2–1.9)	Age, stage	Age (>60 yrs), Stage IV disease
Wudel et al. (2002)	Tennessee	642	16	1990–2000	University medical center, city hospital	Evaluated survival differences between AA and Caucasian patients	HRNE; greater survival for Caucasians	Kaplan–Meier survival estimates stratified by hospital, race, stage, therapy	HRNE
Clegg et al. (2002) ³	U.S. (SEER)	11,796	8	1988–1997	SEER Program data	Assessed survival rates among U.S. Caucasian and minority patients with CRC	Males: 1.2 (1.2–1.3); females: 1.2 (1.1–1.2) ^e	Age, stage (for each gender)	Multivariate analysis of other prognostic factors not reported
Marcella and Miller (2001) ⁸	Pennsylvania	61,804	6	1987–1993	State tumor registry	Assessed racial differences in mortality based on stage at presentation and stage-specific mortality rates.	1.19 (1.09–1.30)	Gender, age, stage, site, grade, SES	Increasing age; male gender; AA × female interaction; tumor stage, site, and grade declining SES

(continued)

TABLE 1
(continued)

Study (yr)	Location of study population	No. of patients in study population	% AA patients	Yrs diagnosed	Source of patient data	Descriptive study notes	HR (95% CI) ^a	Variables included in multivariate analysis ^b	Other statistically significant variables in multivariate analysis of survival
Roetzheim et al. (2000) ¹¹	Florida	9548	6 (9% Hispanic patients)	1994	State tumor registry	Examined the effects of health insurance, race, and aftercare on outcomes of patients with CRC	1.18 (1.01-1.37)	Age, gender, sociodemographics, stage, site, treatment, smoking, comorbidity index	Increasing age, males, marital status, non-Medicare insurance, low education, increasing comorbidity index, smoking, tumor stage, treatment modality
Merrill et al. (1999) ¹⁰	Seattle WA; SF/Oakland, CA	15,352	6 (6% other patients of nonwhite race/ethnicity)	1985-1992	SEER Program data	Compared treatment use and long-term survival of patients with CRC between Medicare beneficiaries in HMOs and fee-for-services programs	Race: 0.99 (0.88-1.12);	Age, gender, region, insurance, education, stage, site, comorbidity	Increasing age, region (Seattle vs. SF/Oakland), lowest education level, tumor stage, comorbidity index, site
Dominitz et al. (1998) ⁶	US VA hospitals	3176	18	1989	Patient treatment files from VA hospitals	Evaluated the influence of race on treatment and survival of patients with CRC in an equal-access medical system (VA hospitals).	1.13 (1.01-1.28)	Age, VA status, VA region, comorbidity, distant metastases, site	Age (> 79 yrs), increasing comorbidity score, presence of distant metastases, tumor location
Cooper et al. (1996) ⁴	U.S. Medicare beneficiaries	81,579	7	1987	Medicare provider analysis and review	Examined survival differences in older Medicare patients (age > 65 yrs)	HRNE; OR: 1.38 (1.3-1.5)	Age, gender, comorbidity, extent and location of disease	Multivariate analysis of other prognostic factors not reported

AA: African-American; HR: hazard ratio; 95% CI: 95% confidence interval; VA: Veterans Affairs; CAC: colonic adenocarcinoma; NSABP: National Surgical Adjuvant Breast and Bowel Project; SF: San Francisco; CCPDS: Centralized Cancer Patient Data System; SES: socioeconomic status; CRC: colorectal carcinoma; HRNE: HRs were not estimated; OR: odds ratio.

^a AA vs. Caucasian (other measures of association as indicated).

^b Race was included in all multivariate models.

^c Confidence intervals were not reported.

^d Estimated from their analyses.

^e Non-Hispanic white males and females were the referent groups in this study.

pared using the log-rank test.¹⁹ Separate curves were generated to estimate survival at 5 years and 10 years postsurgery for patients with colon carcinoma (proximal or distal) and patients with rectal carcinoma. A priori, we chose to analyze survival outcomes for patients with colonic adenocarcinoma (CAC) and rectal adenocarcinoma separately, because we felt that survival according to race in patients with tumors located in these two distinct anatomic sites may have different prognostic factors. Subsequently, we evaluated effect modification by tumor site (colonic vs. rectal) between race and stage while controlling for all other variables. Cox proportional hazards models were used to estimate the hazard ratio (HR) of death due to both colon carcinoma and rectal carcinoma for African Americans compared with Caucasians.²⁰ In that analysis, we controlled for race, age, gender, hospital, anatomic subsite, tumor stage, and tumor grade. These models were generated separately for 5-year and 10-year survival periods. Using Cox regression, we estimated the HR of death due to colon carcinoma for African Americans compared with Caucasians, with stratification by tumor stage at diagnosis. All analyses were performed with SAS statistical software (Version 9.0; SAS Inc., Cary, NC).^{21,22}

RESULTS

The average age of the study population at the time of diagnosis was 64.8 years; there were more males (60%) in the study population, because 31% of the cohort ($n = 155$) was treated at the VA hospital, where the majority of patients are men. Demographic and tumor characteristics for African-American and Caucasian patients are shown in Table 2. There were no significant differences by race with regard to age ($P = 0.47$), treatment hospital ($P = 0.87$), tumor stage ($P = 0.77$), or tumor grade ($P = 0.17$). Distribution of tumors based on anatomic location within the colon/rectum ($P = 0.05$) differed significantly between groups, with African Americans being more likely to present with proximal tumors and less likely to present with distal or rectal tumors compared with Caucasians. After excluding rectal malignancies, this difference in tumor sites ($P = 0.10$) was attenuated (Table 2).

Survival Analyses

African Americans with CACs had poorer 5-year (log-rank test: $P = 0.01$) and 10-year survival rates (log-rank test: $P = 0.02$) compared with Caucasians (Fig. 1). The proportion of patients lost to follow-up (censored) was similar in both racial groups. Within 5 years postsurgery, 16% of Caucasians ($n = 35$) and 12% of African Americans ($n = 19$) were lost to follow-up, and within 10 years postsurgery, 31% of Caucasians ($n = 68$) and

TABLE 2
Demographic and Tumor Characteristics of 491 Patients with Colorectal Adenocarcinoma Who Underwent Surgical Resection

Variable	No. of patients (%)		P value
	Caucasians ($n = 292$)	African Americans ($n = 199$)	
Gender			
Male	190 (65.1)	108 (54.3)	0.02
Female	102 (34.9)	91 (45.7)	—
Age group (yrs)			
0–49	35 (12.0)	17 (8.5)	0.47
50–64	103 (35.3)	72 (36.2)	—
≥ 65	154 (52.7)	110 (55.3)	—
Hospital			
University	199 (68.1)	137 (68.8)	0.87
Veterans Affairs	93 (31.9)	62 (31.2)	—
Stage			
I	60 (20.6)	41 (20.6)	0.77
II	106 (36.3)	72 (36.2)	—
III	88 (30.1)	54 (27.1)	—
IV	38 (13.0)	32 (16.1)	—
Tumor grade			
Poorly differentiated	33 (11.3)	34 (17.1)	0.17
Moderately differentiated	212 (72.6)	132 (66.3)	—
Well differentiated	47 (16.1)	33 (16.6)	—
Anatomic site ^a			
Proximal	111 (38.0)	96 (48.2)	0.05
Distal	118 (40.4)	73 (36.7)	—
Rectal	63 (21.6)	30 (15.1)	—
Colonic subsite ^b			
Proximal	111 (48.5)	96 (56.8)	0.10
Distal	118 (51.5)	73 (43.2)	—
Vital status (at end of follow-up)			
Alive	86 (29.5)	44 (22.1)	0.07
Died of CRC	133 (45.5)	102 (51.3)	—
Died of other causes	73 (25.0)	53 (26.6)	—

CRC: colorectal carcinoma.

^a Proximal sites included the cecum, ascending colon, and transverse colon; distal sites included the descending and sigmoid colon.

^b Included only patients with colon carcinoma (patients with rectal carcinoma were excluded).

26% of African Americans ($n = 43$) were lost to follow-up. There were only 2 deaths (events) among African Americans and 5 deaths among Caucasians after 10 years of follow-up. Patients with rectal tumors were analyzed separately, and no statistically significant racial differences in survival rates were found at 5 years (log-rank test: $P = 0.35$) or at 10 years (log-rank test: $P = 0.30$) postsurgery (data not shown).

We evaluated the influence of tumor location on survival in both groups using Cox regression analysis. In the study population, anatomic tumor site (colonic vs. rectal) was an effect modifier of the relation between race and survival (Fig. 2). Specifically, among patients with rectal carcinoma, Caucasians had poorer 5-year and 10-year survival rates, although these find-

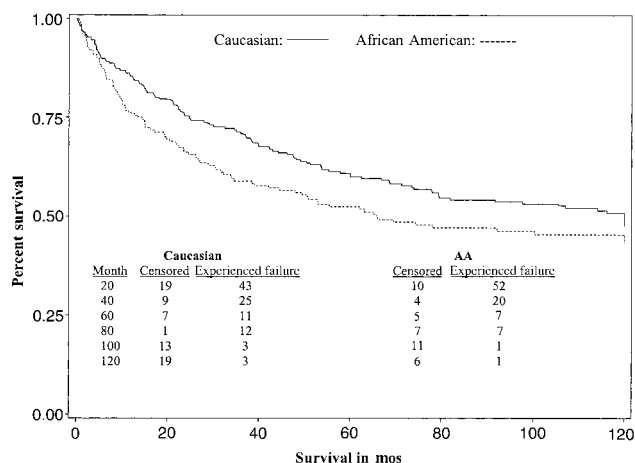


FIGURE 1. Kaplan–Meier survival curves for Caucasian ($n = 221$) and African-American (AA; $n = 163$) patients with colonic adenocarcinomas. Survival rate at 5 years (log-rank test: $P = 0.01$): Caucasian patients, 62.6%; AA patients, 51.5%. Survival rate at 10 years (log-rank test: $P = 0.02$): Caucasian patients, 51.5%; AA patients, 40.9%.

ings were not statistically significant. In contrast, statistically significant differences were found with respect to colon carcinoma: African Americans had poorer 5-year and 10-year survival rates (Fig. 2).

Cox proportional hazards models were used to estimate the adjusted HRs for death due to colon carcinoma. Overall, African Americans were 38% (HR, 1.38; 95% confidence interval [95% CI], 1.03–1.83) more likely to die of colon carcinoma compared with Caucasians. Adding demographic and tumor characteristics to the model increased the magnitude of the HR and the significance level of the race variable (HR, 1.47; 95% CI, 1.09–1.98). Among patients with colon carcinoma, African Americans were 67% (95% CI, 1.21–2.33) more likely to die within 5 years after surgery due to this malignancy compared with Caucasians (Table 3). Within a 10-year period, African Americans had a 52% (HR, 1.52; 95% CI, 1.12–2.07) increased risk of death due to colon carcinoma compared with Caucasians after adjusting for the other variables in the model (Table 3). The attenuation in race-related risk (15% reduction) of death due to colon carcinoma within 5 years postsurgery, compared with 10 years postsurgery, may be attributable in part to increasing age. When patients with rectal tumors were evaluated using multivariate analysis, no statistically significant difference was found in the risk of death due to rectal carcinoma ($P = 0.39$) between African-American patients and Caucasian patients (data not shown).

Cox regression analyses of CACs based on tumor stage revealed disparities in survival between African-

American and Caucasian patients with Stage II, III, and IV adenocarcinomas; however, this association was statistically significant only for patients with Stage II disease (Table 4). Among patients with Stage II CACs, African Americans had a 2.53-fold greater risk of death (95% CI, 1.31–4.86) due to colon carcinoma within 5 years after surgical resection compared with Caucasians. Within a 10-year period after surgery, African Americans with Stage II CACs were 1.82 times more likely to die (95% CI, 1.04–3.18) of this disease compared with Caucasians (Table 4). We could not perform similar survival analyses for patients with Stage I CACs, because not enough events (deaths due to colon carcinoma) occurred among these patients. We also did not perform multivariate analyses of patients with rectal tumors based on tumor stage, due to the limited number of patients in each stage category in both racial groups.

DISCUSSION

We performed survival analyses to elucidate differences in mortality rates between African Americans and Caucasians who underwent surgical resection for CACs and rectal adenocarcinomas. The results of these analyses revealed that compared with Caucasians, African-American patients with CACs had a > 50% greater risk of death due to colon carcinoma within 5 years and 10 years after surgery. Furthermore, among patients with Stage II colon carcinoma, the analysis revealed that African Americans had a 2.53-fold greater risk of death due to colon carcinoma within 5 years after surgery compared with Caucasians. Within 10 years postsurgery, the racial disparity persisted among patients with Stage II disease: African Americans were found to have a 1.82-fold greater risk of death compared with Caucasians. There were no observed racial differences in survival among patients with rectal tumors.

The results of the multivariate Cox regression analyses of CACs indicate that after adjusting for all other variables (including age, gender, hospital, tumor stage, degree of tumor differentiation, and tumor anatomic subsite), the risk of death due to colon carcinoma was significantly greater for African-American patients compared with Caucasian patients. The current study, like many others, indicated that older age at diagnosis, increasing tumor grade (poorly differentiated tumors), and pathologic stage were strong risk factors (Table 1).

Several studies have suggested that survival differences between African Americans and Caucasians may be attributable in part to the disease stage at the time of diagnosis.^{8,9,23,24} African Americans typically present with advanced-stage disease at the time of

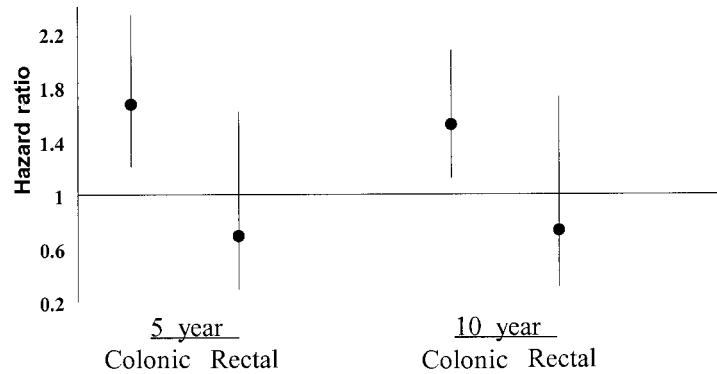


FIGURE 2. Colorectal carcinoma mortality hazard ratios for African-American patients compared with Caucasian patients according to anatomic tumor subsite. Hazard ratios are adjusted for age, gender, hospital, tumor grade, and tumor stage.

TABLE 3
Cox Regression Hazard Ratios for Colon Carcinoma Mortality (Overall and for Five-Year and Ten-Year Survival Periods) among Patients with Colonic Adenocarcinomas Who Underwent Surgical Resection

Variable	Overall survival		5 yr survival		10 yr survival	
	Crude HR	Adjusted HR (95% CI) ^a	Crude HR	Adjusted HR (95% CI) ^a	Crude HR	Adjusted HR (95% CI) ^a
Race						
Caucasian	1.00	1.00	1.00	1.00	1.00	1.00
AA	1.38	1.47 (1.09–1.98)	1.49	1.67 (1.21–2.33)	1.40	1.52 (1.12–2.07)
Gender						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.14	0.99 (0.70–1.41)	1.19	1.02 (0.70–1.50)	1.21	1.00 (0.70–1.43)
Age group (yrs)						
0–49	1.00	1.00	1.00	1.00	1.00	1.00
50–64	1.21	1.80 (1.01–3.18)	1.00	1.52 (0.84–2.77)	1.26	1.84 (1.03–3.29)
≥ 65	1.32	1.97 (1.15–3.36)	1.06	1.59 (0.91–2.76)	1.29	1.91 (1.10–3.30)
Hospital						
UAB	1.00	1.00	1.00	1.00	1.00	1.00
VA	0.89	1.19 (0.81–1.77)	0.85	1.22 (0.79–1.88)	0.92	1.24 (0.83–1.84)
Stage						
I	1.00	1.00	1.00	1.00	1.00	1.00
II	2.13	2.05 (1.14–3.68)	3.14	2.85 (1.27–6.42)	2.40	2.31 (1.24–4.28)
III	4.11	4.24 (2.38–7.53)	7.10	6.59 (2.98–14.56)	4.61	4.66 (2.53–8.57)
IV	15.4	16.4 (9.01–30.0)	24.2	23.22 (10.34–52.1)	16.8	17.66 (9.37–33.3)
Tumor grade (differentiation)						
Good	1.00	1.00	1.00	1.00	1.00	1.00
Moderate	1.26	1.17 (0.75–1.83)	1.57	1.58 (0.92–2.73)	1.32	1.25 (0.78–1.98)
Poor	2.25	1.82 (1.07–3.12)	3.36	2.80 (1.51–5.17)	2.39	1.99 (1.15–3.46)
Colonic subsite						
Proximal	1.00	1.00	1.00	1.00	1.00	1.00
Distal	0.94	0.88 (0.65–1.18)	0.98	0.93 (0.67–1.28)	1.00	0.93 (0.69–1.26)

HR: hazard ratio; 95% CI: 95% confidence interval; AA: African American; UAB: University of Alabama–Birmingham; VA: Veterans Affairs.

^a HRs were adjusted for other variables in the model.

diagnosis and have a poorer clinical outcome compared with Caucasians.^{5,8,9,23–25} Other factors, including treatment issues, differential treatment options, socioeconomic characteristics, and biologic differences, have been proposed as potential explanations for the racial disparity in the survival of patients with CRC.^{4,26–28} In the current study, however, disease stage at diagnosis was distributed similarly for African

Americans and Caucasians and was found not to account for differences in overall survival. When we stratified by disease stage at diagnosis, we found that Caucasians had better survival compared with African Americans in each stage, specifically among patients with Stage II colon carcinoma. Other studies have suggested that differential understaging among racial groups and differences in specialization among phy-

TABLE 4
Cox Regression Hazard Ratios for Colon Carcinoma Mortality among African Americans Compared with Caucasians According to Disease Stage

Variable ^a	Hazard ratio (95% CI)	
	5 yrs	10 yrs
All stages combined ^b		
Caucasians	1.00	1.00
African Americans	1.58 (1.14–2.18)	1.45 (1.07–1.95)
Stage II		
Caucasians	1.00	1.00
African Americans	2.53 (1.31–4.86)	1.82 (1.04–3.18)
Stage III		
Caucasians	1.00	1.00
African Americans	1.21 (0.70–2.12)	1.15 (0.68–1.96)
Stage IV		
Caucasians	1.00	1.00
African Americans	1.44 (0.78–2.64)	1.49 (0.81–2.75)

95% CI: 95% confidence interval.

^a Adjusted for age, gender, hospital, tumor grade, anatomic subsite in the colon.

^b There were not enough events (outcomes) to allow assessment of survival differences among patients with Stage I disease.

sicians at different hospitals may contribute to the survival discrepancy observed between African Americans and Caucasians.^{5,9} However, we had a homogeneous group of physicians (clinical oncologists, surgeons, and pathologists) who diagnosed, treated, and performed staging for all patients at both the UAB and VA hospitals. Therefore, in the current analyses, biases in treatment, diagnosis, and staging between African Americans and Caucasians should be minimal. Thus, it is unlikely that these key characteristics contributed to the racial disparity in survival observed in the current study.

An additional strength of the current study is that all patients underwent uniform treatment with surgical resection. None of the patients were treated with chemotherapeutic agents, such as 5-fluorouracil (5-FU), or with any other neoadjuvant or adjuvant therapy. A recent study suggested that differences in survival by race may be due to differential use of chemotherapy and radiotherapy.⁷ Because surgical resection was the only treatment received by the patients in the current study, differences in terms of compliance with chemotherapeutic regimens did not complicate the results. Moreover, adjuvant chemotherapy was not commonly used at the beginning of the study's time frame (1981), but the use of adjuvant therapy for CRC became more widespread in 1988. The Food and Drug Administration approved leucovorin calcium for use in combination with 5-FU to prolong survival in the palliative treatment of patients

with advanced CRC (Stage IV) in 1952; however, adjuvant treatment in combination with 5-FU after surgical resection in patients with Dukes Stage C colon carcinoma was not approved until 1990. Consequently, the use of 5-FU has become common for the treatment of patients with Stage III and IV tumors. Therefore, the number of patients who received chemotherapy in the initial study was limited. Nonetheless, adhering to the exclusion criteria outlined above (see Materials and Methods), we excluded patients who received presurgical or postsurgical adjuvant therapy. In addition, the same homogenous physician pool provided postsurgery follow-up care for patients at both the UAB and VA hospitals to negate the potential for differential treatment options.

The unique characteristics of the current patient population (African Americans and Caucasians) serve to clarify racial differences in the survival of patients with CACs or rectal adenocarcinomas. First, a significant proportion of patients treated at our medical institutions (~30%) are African American. Second, the study population was homogeneous with regard to treatment (i.e., treatment was similar for patients treated before 1988 and patients treated after 1988). Furthermore, the only treatment received by the study cohort was surgical resection, which is the most effective curative therapy for CRC.^{29,30} This consistent method of treatment may eliminate systematic bias in the current dynamic cohort. Third, variations in physicians' diagnostic and surgical skills did not confound the association between race and survival, because the same pool of physicians diagnosed, treated, and performed staging for African-American and Caucasian patients. These features of the current patient population presented us with the ability to evaluate the true survival history of patients in the two racial groups. Furthermore, our analysis was performed without biases with regard to patient selection, disease stage at diagnosis, and treatment. Using a case accrual period of 1981–1993 and a study follow-up period of 1981–2003, we were able to use a retrospective follow-up design with a dynamic cohort of patients. This allowed us to generate 5-year and 10-year survival patterns without losing data due to right censoring.

An important feature of colorectal neoplasia is its anatomic location within the colon/rectum, which consequently influences the clinical outcome. In the current study, the distribution of CRCs in the proximal colon, the distal colon, and the rectum varied between African Americans and Caucasians in that proximal colon tumors were more common among African Americans. Similar distributions of tumors have been reported previously in several other studies.^{25,31–35} A number of hypotheses have been proposed for the

apparent differences in the distribution of adenocarcinomas within the colorectum, including differences in diet, alcohol consumption, hormone status, socioeconomic status, and physical activity.^{32,36–40} It is likely that there are differences throughout the colon/rectum regarding sensitivity to dietary carcinogen exposure. Indeed, in experimental studies of animals, it has been demonstrated that a diet high in fat (23% corn oil) increased the incidence tumor development in the proximal colon compared with the distal colon.⁴¹ A subsequent study demonstrated that the difference in the incidence of tumors between the proximal and distal colon was attributable to the greater capacity of the distal colon to cope with initial damage to DNA caused by carcinogens.⁴² These findings underscore the importance of studies aimed at elucidating mechanisms of tumor development in relation to tumor site and of the consideration of tumor location in assessing the aggressiveness and the outcome of patients with CRC.

Neoplasias of the colon and the rectum are distinct entities and may follow dissimilar pathogenic pathways,^{43,44} and treatment of rectal adenocarcinomas differs from treatment of colonic adenocarcinomas. The results of the current study confirm previous reports that African-American patients with colonic adenocarcinomas have shorter postsurgical survival compared with Caucasian patients.^{5,9,45} However, in contrast to previous reports,^{5,13,14} we did not find a significant racial difference in survival among patients with rectal tumors. Previous studies suggested that variation in surgeon-related factors may affect outcomes after surgery for rectal carcinoma.⁴⁶ The null results observed in the current study among patients with rectal adenocarcinomas may have been due to uniform treatment (i.e., surgery alone) and postsurgery follow-up care. Most studies of CRC mortality fail to mention the possible implications of effect modification by tumor site. Therefore, overall survival in patients with CRC may have been reported erroneously in several previous studies.

Despite our increased understanding of the molecular pathogenesis of CRC, the process of translating novel information into improvements in clinical approaches to patient care is lacking. In addition, CRC typically is considered a single disease, ignoring the fact that the colorectal region includes three distinct organs—the proximal colon, the distal colon, and the rectum—each with its own distinct embryologic, biologic, histologic, and physiologic characteristics. Therefore, to further elucidate the racial differences in survival among patients with this malignancy, larger studies are required to understand the underlying biologic mechanisms of pathogenesis and progression

of colorectal neoplasia in relation to tumor stage, tumor location, and race. In addition, demographic characteristics and other clinical features must be considered together with tumor stage in predicting the clinical outcomes of patients with colorectal malignancies.

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