Racial-Ethnic Colorectal Cancer Survival Disparities in the Mountain West Region: The Case of Blacks Compared to Whites

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Background: Substantial disparities in colorectal cancer (CRC) survival among racial-ethnic groups, especially between Blacks and Whites, have been extensively documented in the Northeast, California and South of the United States. The purpose of this study was to ascertain the determinants of colorectal cancer racial-ethnic survival disparities in a state of the Mountain West region, Nevada.

Methods: The study population consisted of a cohort of 12,181 men and women with a first primary invasive carcinoma in the colon and rectum diagnosed between 1995 and 2007, identified through the Nevada Central Cancer Registry and followed for vital status until 31 December 2007. Likelihood ratio chi-square statistics were used to compare the socio-demographic and clinical characteristics for race-ethnicity. Cox proportional regression modeling and partial likelihood tests were used to estimate the hazard ratios and assess interaction effects in CRC cause-specific death.

Results: Blacks and Hispanics were more likely to be diagnosed with distant stage disease, 22.4% and 21.5% respectively, compared to 17.9% in Whites. No difference was observed between racial-ethnic groups for diagnoses in regional stage. Univariate analysis yielded a 20.1% higher risk of CRC death for Blacks compared to Whites [95% CI =1.05–1.37]. Adjustment for tumor stage, sex, age, diagnosis period, tumor sublocation, marital status, and economic status in the multivariate model showed a persistently increased risk of CRC death for Blacks (HR =1.17, 95% CI =1.02–1.33) in relation to Whites.

Conclusions and Implications: Survival disparities persisted among Blacks in our study even after adjusting for common demographic and tumor factors. Further determinants of survival disparities between race/ethnicities, such as course of treatment, should be investigated. Additionally, more public health intervention programs should tailor CRC screening awareness towards minorities as well as ensuring equal access to health care and quality treatment. (*Ethn Dis.* 2013;23[1]:103–109)

Key Words: Colorectal Cancer, Survival Analysis, Cox Proportional Hazard Regression, Racial/Ethnic Disparities

Introduction

Colorectal carcinoma (CRC) is the third most commonly diagnosed and second deadliest cancer in the United States.[1–2] For the year 2011, it is estimated that 141,210 new cases in the United States were diagnosed and that 49,380 people died of CRC.[2]

An overall decline in mortality from CRC has been reported since the 1990s for both, men and women.[2,3–5] This is likely due to increasing use of screening procedures such as the fecal occult blood test and/or endoscopy with increased detection and removal of precancerous polyps, which may reduce the risk of CRC mortality by up to 50%.[6] However, screening procedures are routinely used by only 50% of Americans aged ≥50 years.[7] The declining trend in CRC mortality rates is not the same between racial-ethnic groups.[1] Both female and male Blacks have higher age-adjusted mortality rates of CRC compared to Whites for cases diagnosed in 2004–2008.[8] Also, CRC survival disparities have continued to widen between the different racial-ethnic groups.[2,9] Compared to Whites, Blacks have been shown to have lower overall 5-year CRC survival rates, and the differences are largely attributable to the stage of disease at diagnosis.[10–13]

Overall, a 90% 5-year CRC relative survival rate is observed when the cancer is detected at an early localized stage. However, in the United States between 1999 and 2006 only 39% of CRCs were detected at this stage.[2] Furthermore, Blacks and Hispanics are less likely to be diagnosed with CRC at an early stage. Asians, Pacific Islanders and Whites, are generally the most likely racial groups to survive 5-years after a CRC diagnosis.[2]

To our knowledge, the reasons for CRC survival disparities among racial-ethnic groups (particularly Blacks vs Whites) have not been studied in the Mountain West region states: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico and Utah. Between 2000 and 2010 the Mountain West region has experienced the largest population growth of any large region in the United States, 9.7%.[14] Increasingly minority populations are moving to this region with 45% of Nevadans, for instance, classified as non-White.[14] For Blacks, this is particularly interesting, since the immigration into the Mountain West region coincides with the least differential of per capita income in relation to Whites of any region in the United States.[14]

Little is known about racial-ethnic CRC survival disparities in the Mountain West region. As many population groups across the United States and around the world suffer disproportionately from CRC and its after effects, overcoming CRC health disparities is of utmost significance. Using a cohort of patients who had been diagnosed with invasive CRC from 1995 through 2007 and registered in the Nevada Central Cancer Registry (NCCR), the purpose

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METHODS

The study population (n=12,181) comprised all men and women diagnosed with a first primary invasive carcinoma in the colon, rectum or in the rectosigmoid junction from 1995 through 2007, identified through NCCR and followed for vital status until December 31, 2007. The NCCR is the population-based registry that collects and maintains data on all cancer patients within the State of Nevada. The Registry began collecting cancer incidence data in 1979 on all reportable cancers in accordance with the National Program for Cancer Registries (NPCR) and the North American Association of Central Cancer Registries (NAACCR) Standards.

Date and cause of death, which are routinely linked to the NCCR data by the Office of Health Statistics and Surveillance, were obtained from the Office of Health Statistics and Surveillance. Colorectal carcinoma site and morphology were coded according to the International Classification of Diseases for Oncology (ICD-O);[15] CRC cause of death was identified based on the International Classification of Disease-9 (ICD-9) for all deaths occurring during or before 1999, and ICD-10 for deaths in 2000 and after.

Variables

Variables determined at diagnosis that were assessed for prognostic significance for CRC survival included: age, sex, stage, economic status (ES), race-ethnicity, CRC sublocation, marital status, and time-period of diagnosis. Surveillance Epidemiology and End Results (SEER) summary staging (localized, regional, and distant/unknown) was used to categorize the extent of the disease. Age at diagnosis was divided into 5 categories: ≤44, 45–54, 55–64, 65–74, and ≥75 years old. Race-ethnicity was classified into six mutually exclusive categories: Whites, Blacks, Hispanics, Asians, Native Americans, and other/unknown. Tumor sublocation was categorized into proximal tumors (all those proximal to the sigmoid colon and not reachable by flexible sigmoidoscopy), sigmoid colon, unspecified categories of the colon (colon NOS), and rectosigmoid and rectum.

Economic status (ES) is an ecological measure created based on zip code residence at the time of diagnosis. Information from the 1999 US Census median household income and from the Thompson Reuters annual median household income estimates for 2009 were used to create three levels of economic status (high, medium, and low) of similar size in terms of the population numbers covered, in two different periods of diagnosis: 1995–2003 (with $40,000 per year as the cutoff point between low and medium and $55,000 per year between medium and high); and 2004-onwards (with cutoffs at $47,000 and $65,000, respectively).

Statistics

Likelihood ratio chi-square tests were used to compare the demographics, stage of diagnosis and economic status at zip code level for race-ethnicity groups. G-statistic $P<.05$ were considered statistically significant. Survival rates were calculated using the actuarial method (data not shown). Partial likelihood tests were used to estimate the regression coefficients. Test statistic results were reported using Wald Test value and Wald Chi-square P. All analyses were performed using SAS 9.3.

Analyses

A univariate model was first performed to assess the impact of race-ethnicity alone on CRC survival. Interaction effects between sex and marital status at diagnosis was tested to assess their significant effect on survival before building the main effects model. A multivariable model was executed next, to account for all other selected covariates. In the multivariable model, adjusted hazard ratios (HR) and their corresponding 95% confidence intervals (CI) were estimated using Cox Proportional Hazard Regression. To assess independent prognostic importance, each factor included in the model was tested for significance based on the Wald Chi-square test incorporating the appropriate degrees of freedom. Additionally, for each factor, subgroup level hazard ratios were estimated and corresponding Wald Chi-square P were reported.

Cause-specific survival rate, which estimates the likelihood of surviving cancer during a specified time period if CRC is the only cause of death, was used. Cancer-specific survival was defined as the time between the date of diagnosis and either the date of death due to CRC or the last follow-up date, 31 December 2007, whichever occurred first. Patients who died of causes other than CRC or of unknown causes prior to the follow-up date of 31 December 2007 were censored at time of death.

RESULTS

The entire CRC cohort comprised 12,181 cases. Due to low numbers for

Table 1. Patients' demographic and clinical characteristics by race/ethnicity (*N*=12,005)

	White	Black	Hispanic	Asian	*P*[a]
Characteristic	**% (*n*)**	**% (*n*)**	**% (*n*)**	**% (*n*)**	**.03**
Sex					
Male	54.1 (5494)	52.3 (374)	52.7 (372)	46.0 (193)	
Female	45.9 (4670)	47.7 (341)	47.3 (334)	54.0 (227)	
Age group					<.0001
<44	3.5 (355)	5.2 (37)	9.9 (70)	7.1 (30)	
45–54	9.3 (946)	18.0 (129)	15.9 (112)	17.1 (72)	
55–64	19.6 (1997)	28.0 (200)	24.2 (171)	25.5 (107)	
65–74	31.6 (3210)	27.3 (195)	26.6 (188)	28.3 (119)	
≥75	36.0 (3656)	21.5 (154)	23.4 (165)	21.9 (92)	
Marital status					<.0001
Single (never married)	12.5 (1275)	22.4 (160)	14.7 (104)	14.3 (60)	
Married	51.3 (5211)	43.9 (314)	53.8 (380)	57.9 (243)	
Separated/divorced	8.8 (899)	10.6 (76)	9.5 (67)	6.4 (27)	
Widowed	18.7 (1897)	15.1 (108)	13.0 (92)	13.1 (55)	
Unknown	8.7 (882)	8.0 (57)	8.9 (63)	8.3 (35)	
Economic status[b]					<.0001
Low	49.9 (5003)	60.7 (433)	61.7 (432)	43.6 (182)	
Medium	34.9 (3493)	23.0 (164)	25.9 (181)	34.8 (145)	
High	15.2 (1525)	16.3 (116)	12.4 (87)	21.6 (90)	
SEER stage					
Localized	31.9 (3240)	27.8 (199)	29.9 (211)	26.7 (112)	<.0001
Regional	36.5 (3710)	36.4 (260)	35.6 (251)	39.3 (165)	
Distant	17.9 (1820)	22.4 (160)	21.5 (152)	20.0 (84)	
Unstaged	13.7 (1394)	13.4 (96)	13.0 (92)	14.0 (59)	
Tumor sublocation					<.0001
Proximal	41.0 (4165)	51.0 (365)	33.3 (235)	31.9 (134)	
Sigmoid colon	20.1 (2042)	18.7 (134)	25.9 (183)	26.2 (110)	
Rectosigmoid/rectum	27.7 (2813)	18.3 (131)	31.0 (219)	30.7 (129)	
Colon NOS	11.3 (1144)	11.9 (85)	9.8 (69)	11.2 (47)	

Statistics are based off likelihood ratio chi-square.
[a] *P* = G-statistic *P* for chi-square test of differences between racial-ethnic groups.
[b] Economic status unavailable for 154 cases.

some population groups, only the four largest racial-ethnic groups in Nevada were analyzed: Asians, Blacks, Hispanics and Whites, totaling 12,005 cases (Table 1). Overall, it was found that Blacks and Hispanics were more likely to be diagnosed with distant stage disease, 22.4% and 21.5% respectively, compared to 17.9% in Whites. No difference was observed between racial-ethnic groups for diagnoses in regional stage. Univariate analysis yielded a 20.1% higher risk of CRC death for Blacks compared to Whites (95% CI=1.05–1.37) (Table 2). Adjustment for tumor stage, sex, age, diagnosis period, tumor sublocation, marital status, and economic status in the multivariate model showed a persistently increased risk of CRC death for Blacks (HR=1.17, 95% CI= 1.02–1.33) in relation to Whites (Table 3).

Sociodemographic and clinical characteristics stratified by race-ethnicity groups were assessed (Table 1). A total of 5,824 (47.8%) cancer deaths were reported for the period 1995–2007; out of which 3,621 (29.7%) deaths were for CRC. The mean age for CRC diagnoses (1995–2007) was 68.2 years (± SD 12.5). Of all patients in the cohort, 31.4% were diagnosed at the localized stage, 36.4% at the regional stage, 18.4% at the distant stage, and 13.8% were unstaged. Hispanics were more likely than Whites to be diagnosed at a younger age (≤ 44) with 9.9% vs 3.5% for Whites (data not shown).

With regard to clinical variables, Blacks, Hispanics and Asians were more likely than Whites to present with distant stage disease at the time of diagnosis, 22.4%, 21.5%, and 20.0% respectively compared to 17.9% for Whites. While Whites were more likely to be diagnosed at localized stage than other race-ethnic groups with 31.9%, no differences were observed between race-ethnic groups for cases diagnosed at a regional stage (Table 1). Furthermore, Blacks were more likely to be diagnosed

Table 2. Univariate survival analysis results to assess individual prognostic importance

Race-Ethnicity	HR	95% CI for HR		P^a	Alive at Start	Deaths by CRC[b]
		LL	UL			
Ref=White	1.0				10164	3009
Black	1.20	1.05	1.37	.01	715	245
Hispanic	1.05	.91	1.20	.51	706	226
Asian	.98	.82	1.18	.86	420	120

HR, Hazard Ratios; CI, Confidence Interval; LL, Lower Limit; UL, Upper Limit.
[a] Wald *P*.
[b] Deaths by CRC within 5-years of diagnosis.

with proximal tumors than other groups, with 51.1%.

Additionally, Blacks were more likely to be single at the time of diagnosis than other racial-ethnic groups, with 22.4%. While Asians, Hispanics, and Whites were more likely to be married with 57.9%, 53.8% and 51.3% respectively as opposed to Blacks, at only 43.9%. Moreover, Blacks (60.7%) and Hispanics (61.7%) were more likely to reside in areas with low economic status compared to Whites (49.9%) and Asians (43.7%). Asians were more likely to reside in high economic areas with 21.6% compared to Whites or Blacks households, 15.2% and 16.3%, respectively (Table 1).

Survival Analysis

The CRC cause-specific survival unadjusted model showed that Blacks had a significantly increased risk of death (HR=1.20, CI=1.05–1.37, *P*=.006) compared with Whites (Table 2). The interaction effects between sex and marital status were assessed since the influence of marital status for each sex can have a different impact on survival. The findings to this did not yield any significant results. In the multivariate model (Table 3), when simultaneously adjusted for age group, sex, SEER stage, ES, marital status, and sublocation of the tumor, Black race was still significantly associated with increased risk of death. Blacks had a 1.17 increased risk of CRC death compared to Whites.

Moreover, patients diagnosed in regional (HR = 2.63, CI =2.33–2.97) and distant (HR = 10.43, CI = 9.26–11.75) CRC stages had increased risk of CRC death compared with those diagnosed in localized stage.

Compared to the younger age group (≤ 44), patients in the oldest age group (≥75) had increased risk of death (HR=1.84, CI=1.52–2.22). In addition, female patients were found to have a decreased risk of death compared to males (HR=.88, CI=.82 –.95). Individuals who resided in a low-economic status area had increased risk of CRC death (HR=1.18, CI=1.06–1.31) in relation to those residing in areas of high-economic status.

With regard to CRC tumor sublocation, those diagnosed with unspecified categories of CRC had an increased risk of CRC death (HR = 2.00) compared to those with CRC in the proximal. For marital status at diagnosis, being separated/divorced, or widowed was associated with an increased risk of CRC death (HR=1.18, and 1.23 respectively), compared to individuals who were married at time of diagnosis.

DISCUSSION

Our study found that Black race is a persistent predictor of decreased CRC survival even after adjustment for a comprehensive list of survival determinants. Essentially, many studies on CRC survival disparities have been extensively documented in California, Northeast and South of the United States. Of these studies, many show overall poorer survival for Blacks compared to Whites.[16–19] Some studies have found disparities between Blacks and Whites after adjustment of such factors as age, sex, and/or SES.[19–21] Others did find a disparity but they did not adjust for other important variables like sublocation of the tumor, marital status, and economic status.[22–24] Yet, survival disparity between Blacks and Whites is also evident in the fast-growing population and demographically diverse Sunbelt state of Nevada.

Studies have shown that Blacks are less likely than Whites to receive the most appropriate surgery, adjuvant chemotherapy, and radiation treatments after a cancer diagnosis.[25–26] In clinical trial settings, however, when treatment is equal among study groups, racial differences in survival disappear.[27–28] On the other hand, observational studies are inconsistent in their results. Ward et al found that among Blacks, the 5-year CRC relative survival rate is 30% higher among patients who are privately insured compared to those without health insurance.[29] Yet, some studies suggest that Blacks who receive cancer treatment and medical care similar to that of Whites experience similar outcomes.[30] Our study did not assess health insurance factor due to incompleteness of information.

Socioeconomic status (SES) and differences in stage at diagnosis are some of the factors that have been implicated in CRC racial-ethnic survival disparities.[13,31] In fact, stage at diagnosis has consistently been reported as the strongest predictor of excess risk of death for CRC patients.[31] Our study found CRC patients diagnosed in regional and distant stages and those unstaged had increased risks of death compared with those diagnosed in localized stage. Although stage at diagnosis is consistently shown to be more advanced among Black CRC patients

Table 3. Multivariate predictors of CRC survival using Cox Proportional Hazard Modeling

Characteristic							
		95% CI of HR			Group *P*		
	HR	LL	UL	Subgroup *P*	.0003	Alive at Start	Deaths by CRC[a]
Race-Ethnicity							
Ref=White	1.0					10164	3009
Black	1.16	1.02	1.33	.03		715	245
Hispanic	1.09	0.95	1.26	.20		706	226
Asian	1.01	0.84	1.22	.88		420	120
SEER Stage					<.0001		
Ref=Localized	1.0					3762	368
Regional	2.63	2.33	2.97	<.0001		4386	1061
Distant	10.43	9.26	11.75	<.0001		2216	1297
NA/unstaged	7.74	6.79	8.82	<.0001		1641	874
Sex					.0004		
Ref=Male	1.0					6433	1951
Female	.88	.82	.95	.0004		5572	1649
Period of diagnosis					.4843		
Ref=1995–2000	1.0					4961	1770
2001–2007	.98	.91	1.05	.48		7044	1830
Age groups					<.0001		
Ref ≤44	1.0					492	126
45–54	1.06	.86	1.31	.56		1259	335
55–64	1.11	.92	1.35	.29		2475	681
65–74	1.36	1.12	1.64	.0014		3712	1073
≥75	1.84	1.52	2.22	<.0001		4067	1385
Tumor sublocation					<.0001		
Ref=proximal	1.0					4899	1297
Colon NOS	2.00	1.81	2.20	<.0001		1345	797
Rectosigmoid and rectum	.97	.89	1.06	.57		3292	896
Sigmoid colon	.92	.83	1.01	.10		2469	610
Marital Status				<.0001			
Ref=Married	1.0					6148	1766
Single (never married)	1.04	.94	1.16	.41		1599	465
Separated/divorced	1.18	1.05	1.32	.0049		1069	375
Widowed	1.23	1.12	1.35	<.0001		2152	785
Unknown	.57	.49	.66	<.0001		1037	209
Economic status[b]					.0008		
Ref = High	1.0					1818	447
Medium	1.06	.94	1.18	.33		3983	1148
Low	1.18	1.06	1.31	.0022		6050	1950

HR, hazard ratio; CI, confidence limit; LL, lower limit; UL, upper limit; Colon NOS, not otherwise specified; Ref, reference.
[a] Deaths by CRC within 5-years of diagnosis.
[b] Economic status at a zip code level.

compared with Whites, adjustment for stage alone does not explain all of the racial disparity in survival.[31,32] Age at diagnosis has also been reported as another important predictor of survival for CRC patients.[18–19,33–34] Our study found patients in the oldest age group (≥75 years) had increased risk of CRC death as opposed to the younger age group (<44 years). As increasing age can be associated with increasing risk of medical conditions, this may explain the survival disparity seen among age groups in our study.

Furthermore, proximal colon cancers have been shown to become more common as age increases and are associated with poorer survival outcomes.[35–37] Blacks have characteristically shown to be more likely diagnosed with proximal colon cancers than other racial-ethnic groups.[37] Consequently, the inclusion of sublocation in our study model was to take into account the differential distribution between Blacks and other races.

Studies of marital status and CRC survival are scarce.[38] Johansen et al found being married is advantageous towards CRC survival. In our study, patients who

were divorced/separated or widowed had decreased CRC survival as compared to their married counterparts. Our findings showed Asians, Hispanics, and Whites were more likely to be married than Blacks. These findings may suggest the possible influence of family and social support towards CRC survival disparities. In the context of marital status, prevention programs should also look at the importance of social support and social interconnectedness in CRC survival.

Despite being mentioned as one of the determinants for CRC differential survival among race-ethnicities,[25,31] SES is often controversially defined and measured. Schwartz et al found in their study that SES is independently related to CRC stage; both SES and TNM stage accounted for differences in survival between Blacks and Whites with CRC.[39] Using an ecological measure for economic status, our study found living in low-economic zip code areas is associated with increased risk of CRC death, just like other studies.[25,26,31,39]

Our study showed no statistically significant risk of CRC death for patients diagnosed during 1995–2000 versus those diagnosed in 2001–2007 (Table 3). We expected that given the increases of earlier detection and advancement of treatment procedures,[6] those with more recent diagnoses (2001–2007) would have had better survival compared to those with an older diagnosis (1995–2000). However, in contrast with the rest of the nation, our results suggest that those gains have not yet materialized in Nevada.

Low levels of physical activity and metabolic syndrome, which includes obesity, are known to decrease overall CRC survival, and increase the rates of recurrence.[40–41] Studies have shown that Blacks are more likely to be obese and physically inactive than Whites.[42–43] To what extent these and other comorbid conditions contribute to the excess mortality observed in our study for Blacks with CRC is uncertain.

By and large, studies have identified several factors that contribute to racial-ethnic survival disparities including differences in access to early detection, timely and high-quality treatment and supportive care, as well as other comorbidities.[13] Nevertheless, studies are inconsistent in explaining the extent to which different factors other than stage of diagnosis and SES contribute to the overall differential survival among racial-ethnic groups. Our study adjusted for most common sociodemographic and clinical factors.

Our study had several limitations. Firstly, the follow-up of cancer patients in Nevada, just like the majority of other states, is passive; follow-up for cancer data and some out-of-state deaths may be missing. Secondly, the ES variable is an ecological rather than an individual measure. Other limitations include the lack of use of health insurance for which data was unavailable and possible misclassification of cause of death from death certificates.

CONCLUSIONS

Just like in many populous states, we observed marked Black and White survival disparities for CRC in Nevada. Black race was a particularly persistent determinant of CRC survival disparities in our study. The risks of death for Blacks compared to Whites hardly changed, even after adjustment for stage at diagnosis, economic status, sex, tumor sublocation, age, and marital status at diagnosis. The determinant period of diagnosis shows that survival gains for CRC reported elsewhere in the United States have not been observed in Nevada so far, this is in agreement with the low screening rates in the State (BRFSS data not shown). Further determinants of survival disparities, such as course of treatment, should be investigated. Additionally, more public health intervention programs should tailor CRC screening awareness towards minorities as well as ensuring equal access to health care and quality treatment.

Black race was a particularly persistent determinant of CRC survival disparities in our study.

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