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Racial differences in colorectal cancer survival in a safety net hospital

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Abstract

Background—While racial disparity in colorectal cancer survival have previously been studied, whether this disparity exists in patients with metastatic colorectal cancer receiving care at safety net hospitals (and therefore of similar socioeconomic status) is poorly understood**.**

Methods—We examined racial differences in survival in a cohort of patients with stage IV colorectal cancer treated at the largest safety net hospital in the New England region, which serves a population with a majority (65%) of non-Caucasian patients. Data was extracted from the hospital's electronic medical record and the survival differences among different racial and ethnic groups were examined graphically using Kaplan-Meier analysis. A univariate cox proportional hazards model and a multivariable adjusted model were generated.

Results—Black patients had significantly lower overall survival compared to White patients, with median overall survival of 1.9 years and 2.5 years respectively. In a multivariate analysis, Black race posed a significant hazard (HR 1.7, CI 1.01-2.9, p = 0.0467) for death. Though the response to therapy emerged as a strong predictor of survival (HR = 0.4, CI = 0.2-0.7, p = 0.0021), it was comparable between Blacks and Whites.

Conclusions—Despite presumed equal access to healthcare and socioeconomic status within a safety-net hospital system, our results reinforce the findings from previous studies regarding lower colorectal cancer survival in Black patients, and point to the importance of investigating other risk factors including genetic and pathogenic differences.

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Keywords

racial disparity; African American; blacks; colorectal cancer; survival

1.1 Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed and third most common cause of cancer mortality in both women and men in the United States (US), with an estimated 134,490 new cases and 49,190 deaths in 2016 [1]. CRC mortality in the US has decreased by about 50% between the years 1975 to 2012, possibly due to increased screening procedures and perhaps better oncological management [2]. However, some reports have indicated a higher reduction in mortality favoring Whites when compared to Blacks [1,3–7]. For example, according to Surveillance, Epidemiology, and End Results (SEER) data from 2008 to 2012, the Black population had the highest CRC incidence and mortality, and most significant decline in mortality was noted in White patients compared to all other racial groups [1].

Biological and molecular risk factors as well as differences in socioeconomic conditions and health care access have been implicated in causing racial CRC mortality disparity [8]. Many factors such as obesity, smoking, diets high in fat and red meat, alcohol use, and low vitamin D may contribute [9–12]. We are now understanding that there may be differences in tumor biology between racial groups; Blacks tend to be diagnosed with CRC at a younger age, present with more proximal, advanced, and aggressive tumors, and are more likely to have KRAS mutations [13–18]. Importantly, healthcare access inequality can lead to suboptimal screening [19], late diagnosis, and underutilization of recommended treatments. Racial differences in fear and mistrust of the healthcare system, and also in health literacy needs to be recognized [20–22].

Many studies on the subject of CRC racial survival disparity reported observations stemming from large database analyses without specific clinical, tumor, socioeconomic or treatment information. Also, a majority of epidemiological research was done in a White-dominant population. Moreover, there is a dearth of recent racial disparity studies performed in the era of new biologic agents developed for the treatment of metastatic CRC (bevacizumab, cetuximab and panitumumab). Lastly, as unequal access to healthcare has emerged as a significant contributor to poor survival of Blacks in several studies [18,23], we therefore sought to assess the influence of race on CRC mortality outcomes while minimizing the confounding effect of healthcare access and insurance coverage at an urban, academic safety net hospital consisting of a substantial proportion of Black patients.

1.2 Methods

This was a retrospective observational cohort study of stage IV CRC patients treated between January 1st 2004 and December 31st 2014 at the Boston University Medical Center (BUMC), the largest safety-net hospital in the New England area serving a diverse racial population of patients. During this period, out of total 13, 043 patients either diagnosed or treated for solid organ cancers at Boston Medical Center, 651 patients had CRC (Table 1).

Non-caucasians consisted of almost half (47%) of those cases. Approval from the institutional review board at the Boston University School of Medicine was obtained beforehand. About 65% of the patients treated for metastatic CRC during this time period were non-White. Of the 9,849,135 total patient visits to BUMC during this time period, only 1.51% were uninsured visits without any financial assistance. 36.86% of these visits were Medicaid and 13% were charity. Patient data was obtained from our hospital's electronic medical record (EMR).

1.2.1 Study population and data collection

The study population (n = 147) comprised of patients presenting with stage IV CRC or with initial early stage CRC who later developed stage IV disease. The hospital cancer registry was used to obtain demographic features, date of diagnosis, AJCC staging, primary site of the cancer, and tumor histology. Primary site was categorized into 3 groups; right sided (cecum, ascending colon), left sided (descending colon, sigmoid, rectal) and others (transverse colon and appendix). Chart review was performed using the hospital's EMR system to collect data that were not available through the cancer registry. These included information such as self-identified race, disease burden, mutation status of the tumor, and response to chemotherapy. The primary outcome of interest was overall survival by race. We addressed possible confounding factors known to affect survival, which were: age, gender, Charlson comorbidity index (CCI), body mass index (BMI), presence of metastasis at the time of presentation, carcino-embryonic-antigen (CEA) level at presentation, primary site and tumor histology. Treatment-related factors were also analyzed including response to first line treatment.

At BUMC, KRAS and BRAF mutation testing was included in the standard evaluation of patients with CRC from 7/18/2008 onwards. MSI testing also was part of our standard pathologic evaluation from 2007 onwards. KRAS analysis was performed via PCR in which PCR products were cycle sequenced with ABI BigDye® 3.1 cycle sequencing kit. Capillary-electrophoresis was performed on Genetic Analyzer 3130 and analyzed with sequencing analysis software 5.3.1. As for BRAF analysis, AS0-PCR was performed in duplicate with different DNA concentrations. PCR products were run in a 3% agarose gel and mutation status were compared and assayed with a positive and negative control. MSI testing was performed by immunohistochemical staining for 4 proteins in tissue sample: MLH1, MSH2, MSH6, and PMS2. MSI-PCR was performed with fluorescent labeled primers of BAT25 (6FAM-blue), BAT26 (NED-black), D5S346-APC (HEX-green), D2S123 (FMA) and D17S250 (HEX). PCR products were capillary-electrophoresed on ABI Genetic Analyzer 3130 and analyzed with GeneMapper4.0 software. The EGFR inhibitor cetuximab was first approved for treatment of metastatic CRC in 2004. This recommendation was updated in 2009, as it was found not to be effective in patients with KRAS mutant tumors [24,25]. In 2012, the US Food and Drug Administration (FDA) granted approval for cetuximab to be used in combination with chemotherapy for first-line treatment of KRAS wild-type (WT) metastatic CRC. The FDA concurrently approved the Therascreen® KRAS RGQ PCR Kit, establishing testing of tumor tissue for KRAS mutations as a standard of care. More than 75% of our patients were tested for KRAS even when it was not the standard of care at the time. Bevacizumab, approved in 2004 for first-line metastatic CRC treatment was also

approved for second-line use in 2006. CEA testing was done at diagnosis and at regular intervals to assess for response to treatment or disease progression. It was performed using the Abbot Architect CEA Assay by Chemiluminescent Microparticle Immunoassay (CMIA), a modified and advanced form of ELISA.

Chemotherapy regimens have evolved over time and were incorporated as part of the standard of care at BUMC upon their FDA approval. We grouped first line chemotherapy regimens into three classes based on the combination of chemotherapeutic agents and biologics. Regimen I is defined as a regimen containing fluoropyrimidine based doublet plus a biologic agent (bevacizumab or EGFR inhibitor). Regimen II is defined as fluoropyrimidine based doublet without a biologic agent, and Regimen III included all other combinations.

The response to therapy was categorized based on standard AJCC criteria and grouped as complete response, partial response and stable disease [26]. Response to 1st line chemotherapy was categorized as response (complete or partial response or stable disease) versus no response (as progressive disease).

1.2.2 Statistical analysis

Summary statistics are presented for all study variables including the mean +/− SD for continuous variables and N (%) for categorical variables. Comparisons were done using ANOVA and Chi-squared tests as appropriate. The median and range are reported for survival time. Kaplan-Meier survival curves by race are also presented. For the primary outcome of survival, each demographic and clinical predictor was first examined in a univariate cox proportional hazards model with hazard ratios and 95% confidence intervals reported. Any predictor significant in the univariate model at the $p < 0.1$ level was considered a potential confounder and was included, along with race, in a multivariable adjusted model. A similar approach was used for the outcome of response to first line treatment with logistic regression as the modeling method and odds ratios reported. In these analyses, chemotherapy was classified as combination chemotherapy without biologics, combination chemotherapy with a biologic agent, and ‘other’ chemotherapy. In adjusted analyses, $p<0.05$ was considered statistically significant. Analyses were performed using Matlab 2016a (Mathworks Inc.) and SAS v9.4.

1.3 Results

1.3.1 Baseline characteristics and treatments received

A total of 147 patients with metastatic CRC were identified; 117 patients (79.6%) presented with stage IV disease whereas 30 patients (20.4%) initially presented with early stage disease and later developed stage IV disease. Of the 147 patients, 41.5% were Black, 35.4% were White, 14.3% were Hispanic/Latino (HL), and 8.8% were from other racial groups (including Asians). Baseline characteristics are listed in Table 2. We observed non-significant trends of various differences in baseline features among the different racial/ethnic groups. Though similar proportions of Blacks (24.6%) and Whites (23.1%) presented with right-sided tumors, HL patients had lower incidence of right-sided tumors (14.3%). There

was a higher percentage of signet ring and mucinous types of CRC in Black patients (11.5%) compared to Whites (7.7%) and this aggressive phenotype was least among HL patients (4.8%). A higher number of Black patients presented with stage IV disease (86.9%) and also had a higher number of total metastatic sites compared to other racial groups. CEA was measured at the time of presentation in all CRC patients. Using a cut-off of 275 ng/ml, as described by Dixon et al, we observed that 26.2% of Black patients have pre-treatment CEA levels of > 275 ng/ml and only 11.5% and 9.5% of White and HL patients respectively had CEA levels > 275 ng/ml [27].

We then examined molecular markers among our CRC cohort. More than 75% of patients were tested for KRAS; 44.44% of Black patients had the KRAS mutation in codon 12 or 13, compared to 32.4% and 22.2% of White and HL patients respectively. On the other hand, BRAF analysis was performed in only 39.45% of patients as it was adopted in the clinical work up of patients since 2008 at our institution. Even with this limitation, none of the patients were reported to have a BRAF mutation. Close to half of all patients (44.22%) had MSI analysis (adopted in 2007 at BUMC). However, all tested Black patients had MSS tumors, whereas the incidence of MSI tumors was noted to be highest in the HL group at 18.18%.

Treatment-related parameters were compared as shown in Table 3. Debulking surgery and/or metastasectomy were performed in 23.8% and 15.4% of patients in the HL and White groups respectively. In contrast, only 11.5% of Black patients underwent these procedures; however this difference did not reach statistical significance. In addition, a higher number Black patients (45.9%) did not undergo surgical intervention compared to the White (32.7%) and HL (33.3%) patients, likely related to the fact that Black patients have more advanced disease at the time of presentation.

We observed that the highest number of HL patients (61.9%) received Regimen I as 1st line treatment, compared to 50.8% of Blacks and 46.2% of White patients. Among 71 patients with KRAS wild type (WT) tumors, only 40 patients received EGFR inhibitor therapy as first line therapy. Among all racial groups, HL patients (71.4%) were most often treated with an EGFR inhibitor, compared to 60% in Black and 48% in White patients. In contrast, the percentage of patients treated with bevacizumab was very similar among all the racial/ethnic groups. None of these differences reached statistical significance.

Intriguingly, HL group had the highest overall response rates (76.2%) compared to Blacks (62.3%) and Whites (59.6%) groups; however, this difference did not reach statistical significance.

1.3.2 Overall survival

Differences in overall survival were observed across racial groups. Median (range) survival was 1.9 years (0 – 5.2 years) in Blacks, 2.5 years in Whites (0 – 11.6 years), whereas HL patients showed higher survival at 3.2 years (0 – 7.2 years). A small group of patients made up of Asians and those without racial information were grouped as ‘others’ (8.8% of total cohort), who had median survival of 5.2 years (0.4 – 8.1 years).

The adjusted and unadjusted results of the Cox models are presented in Table 4. In the unadjusted model, the risk of death across racial groups was significantly different (p = 0.0234) with Blacks having a significantly higher risk of death compared to Whites (HR = 1.6, p = 0.0343). Though the HL and "other" groups had lower risk compared to Whites, these differences did not reach statistical significance. Compared to CCI of 9+, the risk of death significantly differed among various groups of CCI (p = 0.0036). Patients with lower CCI (< 7) had significantly lower risk (p = 0.0172) of death while patients with CCI 7 or 8 had a HR of 0.7, which did not reach significance. Patients who exhibited response to 1st line treatment showed a significantly lower risk of death (HR = 0.3, p = 0.0005) compared to those who did not respond. Of note, in univariate analyses, gender, age, site of the primary lesion, tumor histology, presence of metastasis at the time of diagnosis and pre-CEA did not have significant effect on HR for death; however, age and BMI met the p<0.1 criteria for inclusion in the adjusted model. In the adjusted model, Black patients continued to have a statistically significantly higher risk of death (HR of 1.7, p = 0.0467). Response to 1st line chemotherapy also continued to significantly influence CRC survival (HR 0.4, p = 0.0021).

1.3.3 Response to first line treatment

We further probed the predictors of response to 1st line therapy to examine specifically the influence of race. The unadjusted model was created considering all the above parameters along with the type of 1st line chemotherapy. The latter parameter was sub-grouped as chemotherapy (others), combination chemotherapy without biologics and last subgroup as combination chemotherapy with a biologic agent. The type of chemotherapy had a significant effect on response (p = 0.0192). The odds ratio (OR) of response was found to be significantly higher in the group that received chemotherapy with one biologic agent (OR = 3.4), yet it did not reach statistical significance. However, no difference in the response rate to first line therapy was noted among different racial groups.

1.4 Discussion

Our study, centered at an academic safety net hospital with a large non-White population, demonstrated a significant influence of race on metastatic CRC survival after adjusting for known confounding variables. While response to first-line chemotherapy emerged as a strong and independent predictor of overall survival, Black patients still had poorer survival despite no perceived differences in treatment response rate when compared to other racial groups.

Krain et. al., first reported an increase in CRC mortality among non-White patients from California in 1972 [28]. This finding was attributed to increasing socioeconomic status and a more affluent diet [29]. Over time, CRC mortality has decreased in White patients. In the Black population, mortality initially increased, but decreased since the 1990s, albeit to a smaller degree [1]. It is unclear if this disparity is confined to any specific stage of disease, with contrasting results in various studies [6,30]. Lower socioeconomic status is a well-known major source of health disparity, and also a major confounding factor; more Blacks live in poverty and do not have health insurance compared to Whites [2]. Simpson and coworkers demonstrated that Black patients had lower rates of surgical, medical and

radiation oncology consultations and received less systemic chemotherapy and local therapy [31]; Black patients in this study had a 15% higher risk of death compared to Whites but this risk vanished after adjustment for treatment differences. A retrospective secondary-data analysis of the California Cancer Registry also showed that better quality care may eliminate colon cancer outcome disparities [32]. Our study addresses socioeconomic status and healthcare access as a confounding factor. This is because BUMC is an academic safety net hospital, which is ideally positioned to allow equal access to healthcare for a patient population with low socioeconomic status regardless of race. In addition, because of healthcare reform in Massachusetts, patients have the nation's lowest uninsured rate. Therefore, very few patients seen at BUMC between 2004-2014 were uninsured and without payment assistance (5.13%).

It is also likely that the differences in the screening and surveillance may contribute to the higher mortality in blacks compared to other racial population. Screening is an important variable, as it is a modifiable factor in influencing the stage of presentation of colorectal cancer, which in turn influences mortality. In fact, more aggressive screening has been proposed for racial populations with increased risk of poor CRC outcomes [33]. As blacks present at an earlier age [34], the American College of Gastroenterology recommended starting screening colonoscopy at the age of 45 for black patients. However, at our institution and also in many others (especially in the primary care setting) the USPSTF guideline that recommends starting screening at the age of 50 regardless of ethnicity is commonly adhered to [35]. While there is rationale for earlier screening in black patients, more evidence based on detailed cost-benefit analysis will allow for wider adaptation of this practice.

Surveillance also has implication on CRC survival. It has been reported that surveillance colonoscopy rates after curative treatment of CRC are lower in black patients [36–38]. This could result in late diagnosis and advanced presentation of a second primary cancer, which in turn enhances the associated risks of surgery and other adjunctive treatments. This aspect was examined in a separate study at our institution, which revealed that surveillance colonoscopy at 1 year after curative surgery was similar among different racial groups [39]. Unmarried patients, those with no or unknown education and patients with more comorbidities had a statistically significant association with delayed 1 year colonoscopy or sigmoidoscopy. Interestingly, surveillance colonoscopy within 3 years of curative surgery was found to be higher in black patients in this study. Lack of information on screening or surveillance represents a potential limitation of this study.

Our study showed no statistically significant difference in the proportion of Black or White patients receiving first-line chemotherapy, for which response was an important, independent predictor of survival (Table 3). This is in concurrence with several other studies [40–42]. Furthermore, the proportion of patients receiving fluoropyrimidine-based chemotherapy plus a biologic agent (bevacizumab or EGFR inhibitor) as 1st line therapy was actually higher in Blacks (50.9%) compared to Whites (46.1%). EGFR inhibitor treatment was also more commonly utilized in Blacks with KRAS WT tumors (60%) compared to Whites (48%). The percentage of patients treated with Bevacizumab was similar in Black, White, and HL groups. However, we observed that Blacks had the lowest metastasectomy and/or debulking surgery rates (11.48%) compared to Whites (15.38%) and HL (23.81%). While this could be

considered as a possible underutilization of surgical treatments, Blacks had a higher tumor burden on presentation (higher pre-treatment CEA and number organs involved), which reduces the feasibility of debulking and/or metastasectomy. Furthermore, Blacks had higher CCI which increases risk of peri-operative morbidity and mortality, possibly affecting the physicians' decision to pursue surgery. In our study, it was not possible to evaluate physicians' rationale of treatment choices. What we can conclude, however, is that despite comparable and adequate first-line chemotherapy treatment, the Black population had poor survival, highlighting the need to understand factors outside of socioeconomics and healthcare access. Although, the lower incidence of debulking surgery in our cohort may be medically justified, its potential contribution to survival disparity cannot be ruled out.

Several biologic factors have been proposed to contribute to lower survival in Black CRC patients. It has been shown that Blacks are more likely to present at a younger age and to have more proximal tumors [13–17]. In line with this observation, our study demonstrated that the average age of Blacks with metastatic CRC (58.66 years) was younger than that of White patients (61.76 years). Black patients had a right-sided tumors in similar proportion compared to the White population (24.60% vs. 23.08% respectively). Right-sided CRCs are associated with poorer prognosis than left-sided tumors[43]. Somatic gene mutations in KRAS, BRAF and MSI are well established and validated factors which can influence survival [44]. Kang and coworkers reported a higher proportion of KRAS mutant tumors in Blacks (37%) compared to Whites (21%), and also a positive association of KRAS mutations with higher grade and more advanced stage [45]. Similarly, Yoon et. al.'s analysis of the Alliance N0147 trial in Stage III colon cancer patients showed higher KRAS mutation in Black patients (44.1%) compared to White patients (34.9%) [46]. Analysis of the same trial associated KRAS mutation with adverse outcomes [47]. Concordant with these studies, we observed a higher percentage of KRAS mutation in tested individuals from the Black group (44.4%) compared to the White group (32.4%). Though it did not reach statistical significance, the contribution of these known molecular tumor differences in the Black patients' poorer survival cannot be ruled out.

Although previous studies have shown similar survival of HL patients compared to Whites [2,48], our study showed a non-statistically significant trend towards better survival in HL patients. The numbers of HL patients in our study was small, and therefore it would be difficult to arrive at a definitive conclusion. This observation could be related to more favorable patient characteristics in the HL racial group. However, the HL group is also diverse, as people of Caucasian, African, or South American race could identify themselves as HL. Our study carries the inherent limitations of a retrospective analysis, which include incomplete documentation or follow-up, which could have affected the results of this study. Yet, it included a significant number of patients from both Black and White racial groups to identify survival differences after controlling for known factors associated with CRC outcomes.

1.5 Conclusion

In a single center retrospective study done at a large academic safety net hospital with a dominant proportion of non-White patients with equal access to healthcare, we observed a

significantly lower overall survival in Black patients compared to White and HL patients, and this difference could not be explained solely by disparity in treatment received or socioeconomic status. We found that although response to first line chemotherapy was a strong and independent predictor of overall survival, Black patients still had poorer survival despite a lack of difference in the response to therapy, comorbidities, BMI or tumor burden at the time of presentation. While our study does not rule out the possibility of molecular differences (i.e., RAS mutation, BRAF mutation, and MSI status), it raises a possibility of other pathogenic factors that may contribute to racial differences [49]. More real-world studies are needed to address in depth the influence of race on CRC progression and survival. Ultimately, we hope that these studies would define future research in CRC etiology and lead to race-specific treatment strategies.

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Biographies

UT, SYL; substantial contributions to conception and design, acquisition analysis and interpretation of data; drafting the article.

JW, VBK: analysis and interpretation of data, revising the manuscript critically for important intellectual content.

KH, MC; revising the manuscript critically for important intellectual content.

VC: substantial contributions to conception and design, acquisition analysis and interpretation of data; revising the manuscript critically for important intellectual content. All authors have reviewed and approved final version to be submitted.

Highlights

- This study conducted in the largest safety net hospital in New England area treating predominantly ethnic minorities with closely 99% insured patients shows poor survival of Black colorectal cancer patients.
- Despite receiving comparable first line treatment and achieving comparable response rates Black colorectal cancer patients exhibit inferior survival compared to White patients.
- Other than health care delivery, this study implicates factors such as pathologic and genetic mediators underlying the racial disparities in colorectal cancer survival.

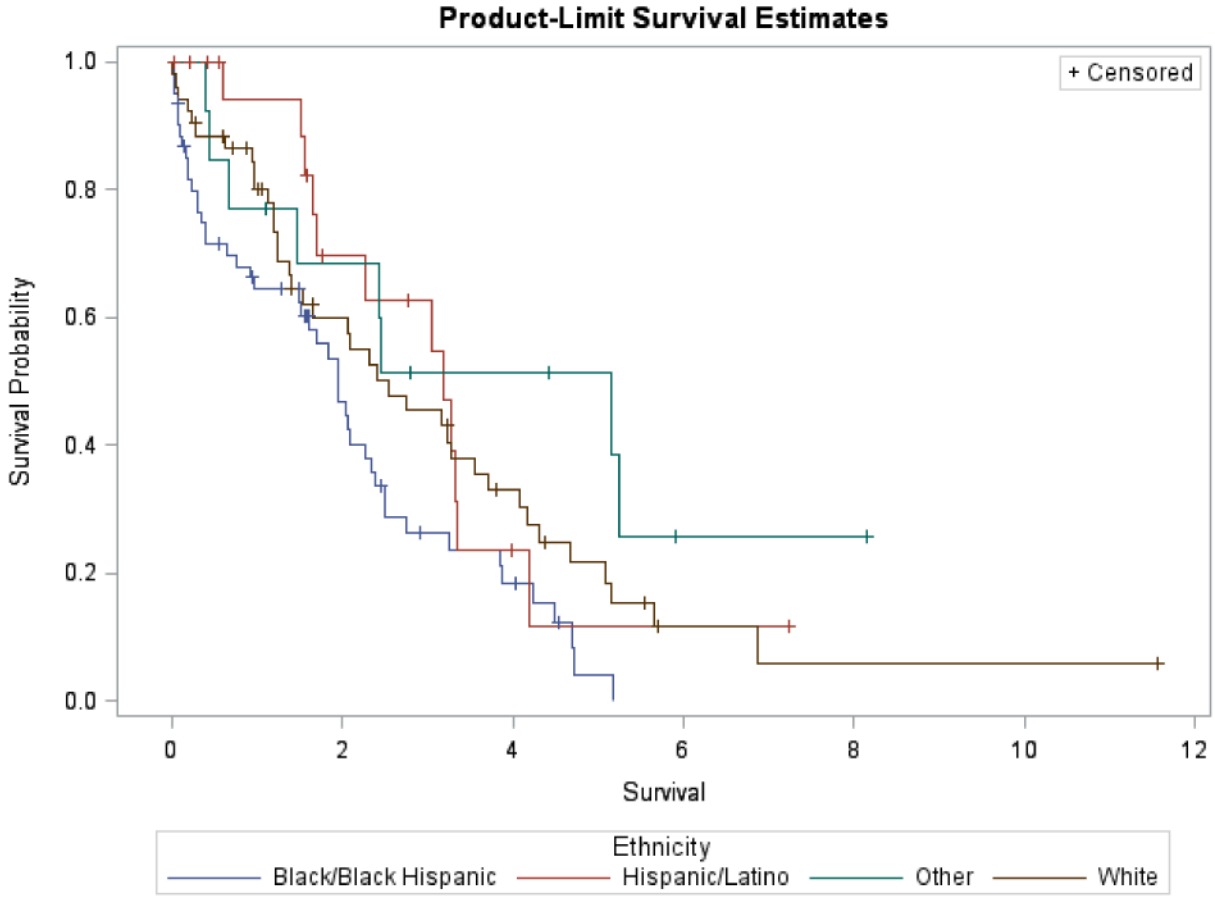

Figure 1. Survival curves for all racial groups

Table 1

Total solid tumor cases treated at BUMC between 2004-2014

Primary site	Blacks	Whites	Others	Total
Brain	17 (14%)	98 (81%)	6 (5%)	121
Ovary	43 (32%)	75 (56%)	17 (12%)	135
Pancreas	96 (32%)	182 (62%)	18 (6%)	296
Colorectal	261 (40%)	343 (53%)	47 (7%)	651
Stomach	121 (40%)	154 (50%)	30 (10%)	305
Lung	443 (27%)	1099 (68%)	88 (5%)	1630
Liver/Intrahepatic Bile Duct	85 (30%)	143 (51%)	52 (19%)	280
Bladder	84 (27%)	210 (66%)	23 (7%)	317
Kidney/Renal Pelvis	144 (32%)	271 (59%)	41 (9%)	456
Other Sites	2905(33%)	5391 (61%)	556 (6%)	8852
TOTAL CASES	4199 (32%)	7966 (61%)	878 (7%)	13043

Table 2

Baseline patient characteristics

	Blacks (n = 61)	Whites (n= 52)	HL (n= 21)	Others (n= 13)
Average age at diagnosis ± SD	58.66 ± 13.02	61.79 ± 14.04	53.53 ± 14.85	64.3 ± 12.55
Gender				
Male (%)	44.26	55.76	47.60	53.8
Female (%)	55.74	44.24	52.60	46.2
Average CCI score ± SD	6.80 ± 1.14	6.73 ± 0.93	6.52 ± 0.87	6.77 ± 1.17
Average BMI ± SD	27.83 ± 7.05	26.99 ± 7.85	27.76 ±5.13	24.69 ± 3.88
Primary site				
Right sided (%)	24.60	23.08	14.29	30.77
Left sided (%)	45.89	55.77	57.14	38.46
Other (%)	29.51	21.15	28.57	30.77
Histology				
Signet ring/mucinous (%)	11.48	7.69	4.76	23.08
Stage IV at presentation (%)	86.89	75.00	76.19	61.54
Average number of organs involved ± SD	1.75 ± 0.83	1.56 ± 0.70	1.52 ± 0.60	1.54 ± 0.66
Patients tested for (n), [%]				
KRAS (113), [76.87%]	45, [73.77]	37, [71.15]	18, [85.71]	13, [100]
BRAF (58), [39.45%]	23, [37.7]	20, [38.46]	9, [42.86]	6, [46.15]
MSI (65), [44.22%]	26, [42.6]	22, [42.3]	11, [52.38]	6, [46.15]
Molecular features				
KRAS mutant (%), [n]	44.44, [20]	32.43, [12]	22.22, [4]	46.15, [6]
BRAF mutant (%),	0	0	0	33.33
Microsatellite instable (%),	0	4.55	18.18	0
Pre-treatment CEA level				
> 275 (%)	26.23	11.54	9.52	0

SD = Standard Deviation, HL = Hispanic, Latino, CCI = Charlson comorbidity index, BMI = Body mass index.

Table 3

Treatment received

	Blacks	Whites	HL	Other
Surgery				
Metastasectomy/Debulking (%)	11.48	15.38	23.81	23.08
No surgery(%)	45.90	32.69	33.33	30.77
Other surgeries (%)	42.62	51.92	42.86	46.15
Chemotherapy				
1st line				
2 agents + biologic (%)	50.82	46.15	61.90	46.15
Other tx's (%)	24.59	32.69	33.33	38.46
No tx (%)	24.59	21.15	4.76	15.38
2nd line				
2 agents + biologic (%)	34.43	46.15	47.62	61.54
Other tx's (%)	27.87	21.15	28.57	15.38
No tx (%)	37.70	32.69	23.81	23.08
EGFR inhibitor tx (for KRAS WT)				
Yes (%), [n]	60, [15]	48, [12]	71.43, [10]	42.86, [3]
Bevacizumab				
Yes (%), [n]	65 . 57, [40]	66.67, [36]	66.67, [14]	69.23, [9]
Chemotherapy response				
1st line *Total # of pts*	61	52	21	13
CR/PR/SD (%), [n]	62 . 30, [38]	59 . 62, [31]	76.19, [16]	69.23, [9]
PD (%), [n]	8.20, [5]	11.54, [6]	14.29, [3]	15.38, [2]

HL = Hispanic, Latino, CR = Complete response, PR = Partial response, SD = stable disease, PD = Progressive disease, tx= therapy

Table 4

Cox proportional hazard models

	Unadjusted			Adjusted**		
	HR	**95% CI**	**P-value**	**H R**	**95% CI**	**P-value**
Race (Ref = White)			(0.0234) *			(0.0612) *
Black/Black Hispanic	1.6	(1.04, 2.5)	0.0343	1.7	(1.01, 2.9)	0.0467
Hispanic/Latino	0.9	(0.5, 1.7)	0.6818	1.2	(0.6, 2.4)	0.6457
Other	0.6	(0.3, 1.3)	0.2008	0.6	(0.2, 1.4)	0.2208
CCI Category (Ref = 9+)			(0.0036) *			(0.1774) *
<6/8	0.4	(0.2, 0.9)	0.0172	0.6	(0.2, 1.5)	0.2687
7/8	0.7	(0.3, 1.6)	0.4210	0.9	(0.3, 2.4)	0.7981
Site Category (Ref = right)			(0.3492) *			
Left	0.8	(0.5, 1.2)	0.2492			
Other	0.6	(0.3, 1.3)	0.2208			
Female Gender (Ref = Male)	1.2	(0.8, 1.8)	0.3767			
Age	1.01	(1.0, 1.03)	0.0632	1.01	(0.99,1.03)	0.4642
BMI	1.0 2	(1.0, 1.1)	0.0994	1.0 2	(0.98, 1.06)	0.3361
Histology: Adenocarcinoma NOS (Ref = Other)	1.1	(0.6, 2.0)	0.6989			
Metastases at Diagnosis	1.2	(0.8, 2.0)	0.4109			
Response (Ref = progression)	0.3	(0.2, 0.6)	0.0005	0.4	(0.2, 0.7)	0.0021
Pre-CEA	1.0	(1.0, 1.0)	0.2215			

*(Overall test of significance for categorical variables with more than 2 categories)

**Race adjusted for variables significant at the p<0.1 level in unadjusted analyses

HR= Hazard Ratio, CCI= Charlson, Comorbidity Index, NOS = not otherwise specified, Pre-CEA = pre-treatment CEA level, HL = Hispanic, Latino