

Colorectal Cancer Survival Disparities among Puerto Rican Hispanics: A Comparison to Racial/Ethnic Groups in the United States

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Abstract

Purpose: Ethnic/racial disparities in colorectal cancer (CRC) survival have been well documented. However, there is limited information regarding CRC survival among Hispanic subgroups. This study reports the 5-year relative survival and the relative risk of death of Puerto Rican Hispanic (PRH) CRC patients compared to other racial/ethnic groups in the US.

Methods: CRC incidence data from subjects ≥ 50 years was obtained from the Puerto Rico Central Cancer Registry and the Surveillance, Epidemiology and End Results (SEER) database from January 1, 2001 to December 31, 2003. Relative survival rates were calculated using the life tables from the population of Puerto Rico and SEER. A Poisson regression model was used to assess relative risk of death by stage, sex, and age.

Results: A total of 76,444 subjects with incident CRC were analyzed (non-Hispanic White (NHW) $n=59,686$; non-Hispanic black (NHB) $n=7,700$; US Hispanics (USH) $n=5,699$; PRH $n=3,359$). Overall and stage-specific 5-year survival rates differed by race/ethnicity. When comparing PRH to the other racial/ethnic groups, PRH had the lowest survival rates in regional cancers and were the only racial/ethnic group where a marked 5-year survival advantage was observed among females (66.0%) compared to males (60.3%). A comparable and significantly higher relative risk of death of CRC was observed for PRH and NHB compared to NHW.

Conclusions: Our findings establish baseline CRC survival data for PRH living in Puerto Rico. The gender and racial/ethnic disparities observed in PRH compared to US mainland racial/ethnic groups warrant further investigation of the risk factors affecting this Hispanic subgroup.

Keywords: Colorectal cancer, colorectal cancer survival, colorectal cancer disparities, racial/ethnic disparities

1. Introduction

Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide, especially in developed countries with a Western culture (Boyle & Langman, 2000; Ferlay J, 2013). In the United States (US), it is the most diagnosed gastrointestinal cancer. The American Cancer Society estimated that 132,700 new CRC cases would be diagnosed and 49,700 deaths due to disease would be reported during 2015 in the US (www.cancer.org). CRC disease burden varies dramatically between races and ethnicities for reasons that remain incompletely understood. A variety of factors, including adherence to routine CRC screening, are thought to contribute to the racial/ethnic disparities observed in CRC incidence and mortality (Gellad & Provenzale, 2010). African Americans have the highest CRC incidence and the lowest survival rates compared to other racial/ethnic groups. When compared to non-Hispanic Whites (NHW), US mainland Hispanics (USH) present more advanced disease and have worse survival (Reyes-Ortiz, Eschbach, Zhang, & Goodwin, 2008; Stefanidis et al., 2006). Furthermore, significant differences in cancer incidence patterns and tumor characteristics have been reported among Hispanic

subpopulation in the mainland US (Pinheiro et al., 2009; Stern, Zhang, Lee, Deapen, & Liu, 2015) suggesting differences in cancer determinants among these subpopulations. Why is this problem important?

Hispanics are the largest and the fastest growing minority ethnic group in the US accounting for 17.1% of the US population (US Census Bureau, 2013); by 2050, it is expected that Hispanics will account for 25% of the US population. However, the term Hispanic does not account for racial differences within the Hispanic population or their country of origin. According to the 2010 American Community Survey (ACS) by the Pew Hispanic Center, individuals self-identified as Mexican are the largest Hispanic subgroup in the US followed by Puerto Ricans (9%) (<http://www.pewhispanic.org>). Cancer is the leading cause of death among USH (American Cancer Society, 2012). CRC is the 2nd most commonly diagnosed cancer and one of the top three causes of cancer-related deaths among USH, making it a major cause of mortality in this population (American Cancer Society, 2012; Varela, Jandorf, & Duhamel, 2010). Although an overall decrease CRC incidence and mortality among USH has been observed (Soto-Salgado et al., 2009), incidence rates are higher among USH than those reported for most Latin American countries. However, there is limited information on CRC survival among the Hispanic subgroups that comprise USH.

According to the 2010 U.S. Census, Puerto Rico (PR) has 3,725,789 residents of which the vast majority (99%) are Hispanics. In PR, CRC is the 2nd most commonly diagnosed cancer and the leading cause of cancer death in men and women (G Tortolero-Luna, 2013). In contrast to the declining CRC incidence and mortality rates reported among USH (Surveillance, Epidemiology, and End Results (SEER) Program 2012), CRC incidence and mortality rates have been increasing in PR Hispanics (PRH) (G Tortolero-Luna, 2013; Soto-Salgado et al., 2009). This may be in part explained by the fact that risk factors for CRC such as obesity and diabetes were reported to be higher in PR compared to the US (Centers for Disease Control and Prevention (CDC), 2012). Genetic ancestry, cultural lifestyle characteristics, and environmental exposures on the island may also contribute to the increasing CRC incidence rates. CRC screening rates, both FOBT and colonoscopies, were reported to be lower among PRH compared to USH, NHB, and NHW individuals in the US (Centers for Disease Control and Prevention (CDC), 2012), making PRH less likely to be diagnosed at an earlier, more treatable stages.

Despite the fact that CRC is the leading cause of cancer death among men and women in PR, information on patient outcomes is limited. To date, stage-specific CRC 5-year survival has not been systematically evaluated in PR. In this study, we report the overall stage-specific CRC 5-year relative survival rates and the relative risk of death by stage, sex and age comparing PRH to USH, NHB, and NHW from national population-based US registries. These analyses will contribute to a better understanding of the differences in CRC survival among Hispanic subgroups and is vital to the implementation of effective, evidence-based health policies in order to reduce CRC morbidity and mortality in this population.

2. Method

2.1 Data Sources

Incidence data from PR was obtained from the Puerto Rico Central Cancer Registry (PRCCR). The PRCCR, one of the oldest population-based registries in the Americas, which was established in 1951 and collects data of newly diagnosed cancer cases in PR. The PRCCR collects demographic characteristics, date of cancer diagnosis, primary cancer site, histological cancer type and method of diagnosis, stage of disease at diagnosis, treatment and follow-up status for patients treated in public and private medical facilities. In addition, the PRCCR obtains information on vital status and cause of death from all incident cancer cases from the Division of Statistical analysis, Auxiliary Secretariat for Planning and Development, from the Puerto Rico Department of Health. Data coding is performed using the standards used by the Surveillance, Epidemiology, and End Results (SEER) program and the North American Association of Central Cancer Registries making PRCCR data fully comparable to data from these registries. Furthermore, the PRCCR meets the North American Association of Central Cancer Registries' silver certification indicating that they have achieved a high standard for complete, accurate, and timely data for calculating standard incidence statistics. All cancer cases diagnosed during the study period (2001-2003) were reported using the 3rd edition of the International Classification of Disease for Oncology (ICD-O) (*International Classification of Diseases for Oncology*, 2000).

Only incident cases with a diagnostic confirmation of primary CRC with histological confirmation (ICD-03 codes: C18.0-C18.9 for colon cancer and C19.9 and C20.9 for rectal cancer) from January 1, 2001 to December 31, 2003 with a follow up until December 31, 2007 were included in our study; only adenocarcinomas were included in this study. Subjects with an unknown method of confirmation were excluded. In situ CRC, subjects with more than one primary tumor, CRC cases diagnosed by death certificate or autopsy only, and cases with no follow-up have been excluded from the analysis (Supplementary Table 1). All subjects in this study were aged 50

years and older. The same inclusion and exclusion criteria were applied to SEER data.

Due to the information available at the PRCCR at the time of the analysis, CRC incidence and mortality data for USH, NHB, and NHW during the period of 2001-2003 were obtained from the SEER program. The SEER 13 program, comprised of 13 population-based cancer registries, covers approximately 14% of the US population (Surveillance, Epidemiology, and End Results (SEER) Program 2012). Individuals of Hispanic ethnicity are identified by a combination of medical record review and matching surnames against a list of Hispanic surnames. In our study, the term Hispanic does not account for racial differences within the Hispanic population. The National Cancer Institute's "Hispanic Index" was used to exclude states where mortality statistics for Hispanics were deemed unreliable (SEER Policy for Calculating Hispanic Mortality). Mortality data was available for all states except Connecticut, Maine, Maryland, Minnesota, New Hampshire, New York, North Dakota, Oklahoma, and Vermont.

2.2 CRC Staging

Stage of disease at diagnosis was categorized based on the SEER Summary Stage 2000 system and was defined as: localized (confined to the primary site), regional (spread to regional lymph nodes and/or by direct extension beyond the primary site), distant (metastatic spread), and unknown stage.

2.3 Statistical Analysis

Demographic characteristics (age and sex), stage of CRC at diagnosis (localized, regional, or distant), primary subsite, histological subtype, histological grade, and type of treatment were analyzed by racial/ethnic group using Chi-square or Fisher's exact test, when appropriate. The 1-, 3-, and 5-year relative survival rates were calculated using the PRCCR incidence case file database and SEER Incidence Database using the Actuarial method (Ederer, Axtell, & Cutler, 1961). Relative survival, an alternative to calculating cancer specific mortality, is calculated as the ratio of the observed survival to the expected survival for a group of people in the general population that is similar to that of the patient group with respect to race, sex, age, and calendar period of observation. Thus, the relative survival of the PR CRC subjects included in this study was calculated using the expected survival of the Puerto Rican population. The observed survival rate is equivalent to the number of patients remaining alive for a specific time-span divided by the total number of patients at risk of death during that specified time period. Expected survival rates were calculated using Ederer II methods (F, 1959) and based on decennial life table for the Puerto Rican population, which takes into account the population distribution of age, sex, and calendar year. Relative survival for CRC was calculated stratified by sex, race/ethnicity and age group; with further sub-analyses performed on the different stages. Survival rates were examined overall and with respect to the following demographic variables: sex (males and females), age group (50-59 and ≥ 60 years), and stage (localized, regional, distant and unstaged). A Poisson regression model was used to assess relative excess risk of death for the racial ethnic/groups studied, after adjusting for sex, age, and stage at diagnosis. Analyses were performed using str in Stata 11.0.

3. Results

3.1 Demographic and Clinicopathological Characteristics of Patients

A total of 76,444 primary CRC diagnosed during 2001-2003 were used in the analyses. Of these cases, 59,686 (78%) were NHW, 7,700 (10%) were NHB, 5,699 (7%) were USH, and 3,359 (4%) were PRH. The demographic and clinical characteristics of the CRC cases included in this study are presented in Table 1. Although the majority of the subjects were diagnosed with CRC at ≥ 60 years in all groups, the median age of CRC diagnosis was higher among NHW (73 years). Similar proportions of males and females were observed in all the racial/ethnic groups studied and the majority of the incident CRC cases were located in the proximal colon. However, both PRH and USH had lower incidence of CRC in the proximal colon and slightly higher incidence in the rectum compared to NHB and NHW.

In general, the tumors were predominantly adenocarcinomas in all racial/ethnic groups. A higher percentage of moderately differentiated colorectal tumors and tumors diagnosed at localized or regional stages were observed in all groups. PRH had a slightly higher percentage of cases at regional stages and the highest percentage of unknown stage cases (13%) when compared with the other racial/ethnic groups. Moreover, a higher percentage of well differentiated tumors (23.7%) and a lower percentage of poorly differentiated tumors (6.3%) were observed in PRH compared to the other race/ethnic groups, which had $< 9.2\%$ and $> 13.4\%$, respectively. Among the individuals diagnosed with CRC during this study period, PRH had the highest percentage of subjects that did not undergo therapy (17.7%) followed by NHB (15.1%).

Table 1. Demographic and clinical characteristics for incident CRC cases diagnosed during 2001-2003 by race/ethnicity.

Characteristics	NHW n= 59,686 n (%)	NHB n=7,700 n (%)	USH n=5,699 n (%)	PRHn=3,359 n (%)
Median age (years (IQR))	73 (63-80)	68 (59-77)	68 (60-76)	69 (61-77)
Age group				
50-59 years	10,315 (17.3)	2,007 (26.1)	1,382 (24.3)	710 (21.1)
60+ years	49,371 (82.7)	5,693 (73.9)	4,317 (75.9)	2,649 (78.9)
Gender				
Male	29,928 (50.1)	3,522 (45.7)	3,034 (53.2)	1,806 (53.8)
Female	29,758 (49.9)	4,178 (54.3)	2,665 (46.8)	1,553 (46.3)
Primary Subsite				
Proximal	25,804 (43.2)	3,539 (45.9)	2,095 (36.8)	1,186 (35.3)
Distal	14,934 (25.0)	1,993 (25.9)	1,530 (26.8)	935 (27.8)
Rectum	16,409 (27.5)	1,783 (23.2)	1,799 (31.6)	983 (29.1)
Other	2,539 (4.3)	385 (5.0)	275 (4.8)	255 (7.6)
Stage at Diagnosis				
Localized	24,021 (40.3)	2,720 (35.3)	2,082 (36.5)	1,086 (32.3)
Regional	22,212 (37.2)	2,755 (35.8)	2,154 (37.8)	1,485 (44.2)
Distant	10,754 (18.0)	1,786 (23.2)	1,178 (20.7)	347 (10.3)
Unknown	2,699 (4.5)	439 (5.7)	285 (5.0)	441 (13.1)
Histologic subtype				
Adenocarcinoma	50,549 (84.7)	6,438 (83.6)	4,745 (83.3)	2,838 (84.5)
Mucinous adenocarcinoma	6,169 (10.3)	734 (9.5)	580 (10.2)	384 (11.4)
Other	2,968 (5.0)	528 (6.9)	374 (6.5)	137 (4.1)
Histologic grade				
Well differentiated	5,266 (8.8)	601 (7.8)	523 (9.2)	796 (23.7)
Moderately differentiated	35,295 (59.1)	4,620 (60.0)	3,336 (58.5)	1,719 (51.2)
Poorly differentiated	10,398 (17.4)	1,035 (13.4)	932 (16.4)	211 (6.3)
Undifferentiated	472 (0.8)	62 (0.8)	34 (0.6)	15 (0.5)
Unknown	8,255 (13.83)	1,382 (18.0)	874 (15.3)	618 (18.4)
Surgery				
No	7,400 (12.4)	1,357 (17.6)	810 (14.2)	735 (21.9)
Yes	52,286 (87.6)	6,343 (82.4)	4,889 (85.8)	2,624 (78.1)
Radiation				
No	53,060 (88.9)	6,961 (90.4)	4,925 (86.4)	2,903 (86.4)
Yes	6,626 (11.1)	739 (9.6)	774 (13.6)	456 (13.4)
Treatment				
No treatment	6,268 (10.5)	1,161 (15.1)	674 (11.8)	594 (17.7)
Only surgery at P-Site	46,792 (78.4)	5,800 (75.3)	4,251 (74.6)	2,309 (68.7)
Radiation and surgery	6,626 (11.1)	739 (9.6)	774 (13.6)	456 (13.6)

3.2 Relative Survival Analysis by Sex

Cumulative relative survival rates for 1-, 3-, and 5-years after CRC diagnosis according to sex and race/ethnicity are shown in Table 2. Differences in relative survival rates for CRC were observed according to race/ethnicity. PRH and USH 1-, 3- and 5-year relative survival rates were comparable to NHW, which had the highest 1-, 3- and 5-year overall relative survival rates after CRC diagnosis. However, when analyzing the data according to sex, PRH was the only racial/ethnic group where a marked 5-year survival advantage was observed among females (66.0%) compared to males (60.3%) (Figure 1).

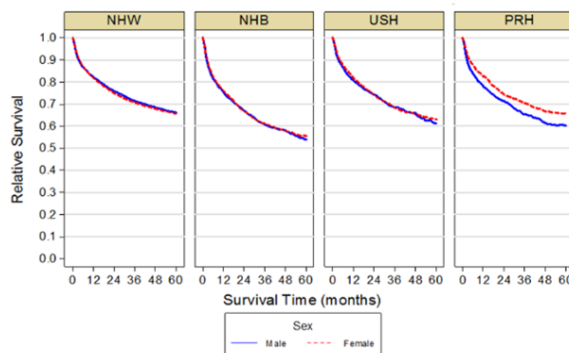


Figure 1. 5-year relative survival for CRC by race/ethnicity and sex. Five-year relative survival rates are shown according to race/ethnicity and sex in individuals older than 50 years diagnosed with incident CRC during 2001-2003 with follow-up through 2007. Males are depicted in blue and females in red dashed lines.

Age-standardization was performed using internal weights

Table 2. 1-, 3- and 5-year relative survival by sex and race/ethnicity for individuals older than 50 years diagnosed with incident CRC during 2001-2003 with follow-up through 2007.

	Male % Survival (CI)			Female % Survival (CI)			Both % Survival (CI)		
	1- year	3-year	5-year	1- year	3-year	5-year	1- year	3-year	5-year
NHW	82.2 (81.5-83.2)	71.5 (70.4-72.7)	66.3 (64.9-67.6)	82.0 (81.2-82.8)	70.8 (69.7-71.9)	65.9 (64.7-67.2)	82.1 (81.5-82.7)	71.1 (70.4-71.9)	66.1 (65.2-67.0)
NHB	75.4 (72.4-78.3)	60.9 (57.1-64.7)	54.0 (49.6-58.43)	76.0 (73.6-78.4)	61.3 (58.3-64.2)	55.6 (52.2-59.0)	75.7 (73.8-77.5)	61.0 (58.7-63.3)	54.8 (52.2-57.5)
USH	80.8 (77.7-83.7)	68.7 (64.7-72.5)	61.2 (56.5-65.9)	82.0 (79.1-84.6)	68.5 (64.9-72.1)	63.2 (58.9-67.3)	81.2 (79.1-83.1)	68.3 (65.7-70.9)	62.1 (59.0-65.2)
PRH	78.2 (74.3-81.8)	65.5 (60.6-70.2)	60.3 (54.6-65.9)	82.6 (78.8-85.9)	70.6 (65.9-75.1)	66.0 (60.6-71.2)	80.4 (77.7-82.9)	67.9 (64.5-71.2)	62.9 (59.0-66.8)

3.3 Relative Survival Analysis According To Age and Stage at Diagnosis

Cumulative 5-year relative survival rates for CRC according to age and stage at diagnosis are shown in Table 3. NHW showed a clear *higher* CRC survival among individuals 50-59 years old (70.8%) compared to the other racial/ethnic groups which had comparable 5-year relative survival rates in this age group. However, a marked *lower* 5-year relative survival was observed in NHB older than 60 years (54.3%) whereas the survival rates in PRH, USH, and NHW were comparable.

When combining both sexes, cumulative 5-year relative survival rates for CRC according to stage at diagnosis were higher in NHW in both localized and regional stages (Table 3). PRH had the *lowest* survival rates in regional cancers (59.3%), but the highest in distant cancers (16.8%) compared to the other racial/ethnic groups studied. PRH had significantly lower 5-year survival rate (85.0%) compared with USH (90.0%) for localized CRC. Comparable survival rates were observed in PRH (85%) and NHB (83%) in individuals diagnosed at localized stages.

Similar rates are observed when analyzing the cumulative five-year relative survival according to sex and tumor stage at diagnosis. In both male and females, two patterns were observed for localized tumors. PRH and NHB had lower survival rates compared to USH and NHW. In PRH males, 5-year relative survival rates for regional disease are the lowest compared to the racial/ethnic groups studied (57.8%). In females, survival rates are close to 61% and are comparable to NHB. For distant stage cancers, PRH have higher survival rates compared to the other racial/ethnic groups in both sexes. However, 5-year survival rates were higher in PRH females (20%) than in males (14%).

Table 3. 5-year relative survival for CRC by race/ethnicity according to age and tumor stage at diagnosis of incident CRC during 2001-2003 with follow-up through 2007.

Characteristics	NHW % Survival (CI)	NHB % Survival (CI)	USH % Survival (CI)	PRH % Survival (CI)
Age group				
50-59 years	70.8 (69.8-71.7)	61.1 (58.7-63.5)	63.3 (60.5-66.0)	65.2 (61.3-68.9)
60+ years	64.6 (64.0-65.2)	54.3 (52.6-56.0)	62.4 (60.5-64.3)	62.3 (59.8-64.7)
Stage at Diagnosis				
Localized	91.3 (90.1-92.7)	83.0 (78.3-87.4)	90.0 (85.0-94.7)	85.0 (78.1-91.2)
Regional	69.4 (67.9-70.9)	61.2 (56.9-65.8)	65.1 (59.9-70.1)	59.3 (53.5-65.0)
Distant	10.1 (9.0-11.2)	7.2 (5.0-10.0)	12.0 (8.5-16.4)	16.8 (9.8-26.3)
Unknown	42.4 (38.4-46.5)	36.0 (26.8-45.9)	45.8 (34.4-57.3)	57.6 (47.3-67.7)

3.4 Relative Risk of CRC Death According To Race/Ethnicity

After adjusting by sex, age and stage at diagnosis, we observed a significantly higher relative risk of death of CRC for PRH (RR=1.28; CI 95%: 1.09-1.28) and NHB (RR=1.27; CI 95%: 1.22-1.32), compared to NHW (Table 4). However, USH show a non-significant lower relative risk of death of CRC (RR=0.98; CI 95%: 0.94-1.04) compared to NHW.

Table 4. Relative Risk of Death for CRC cases by race/ethnicity for all tumor stages combined for individuals older than 50 years diagnosed with incident CRC during 2001-2003 with follow-up through 2007.

Race	Unadjusted Relative Risk of Death	*Adjusted Relative Risk of Death
NHW	1.0	1.0
NHB	1.16 (1.11-1.22)	1.27 (1.22-1.32)
USH	0.91 (0.87-0.97)	0.98 (0.94-1.04)
PRH	1.14 (1.05-1.22)	1.28 (1.09-1.28)

* Adjusted for sex, age and stage at diagnosis.

4. Discussion

Racial and ethnic disparities in CRC survival have been extensively documented in the US mainland population.

CRC is the 2nd most commonly diagnosed cancer and one of the top three causes of cancer-related deaths among USH, making it a major cause of mortality in this population (American Cancer Society, 2012; Varela et al., 2010). An overall decrease CRC incidence and mortality among USH has been observed (Soto-Salgado et al., 2009); however, a recent study shows that there are differences in cancer incidence patterns and tumor characteristics among Hispanics subpopulations according to their country of origin (Pinheiro et al., 2009; Stern et al., 2015). CRC survival among the Hispanic subgroups that comprise USH has yet to be investigated. Puerto Rican Hispanics are the second largest Hispanic group in the mainland US. However, there is very limited information about patient outcomes in PR where CRC is currently the leading cause of cancer death (G Tortolero-Luna, 2013). In the current investigation, we report stage-specific, 5-year relative survival rates and relative risk death of CRC for PRH compared to USH, NHB, and NHW

Differences in demographic and clinical characteristics were observed when comparing PRH to the mainland US racial/ethnic groups studied. Our study shows that PRH had a comparable median age at CRC diagnosis to the other racial/ethnic groups with the exception of NHW, which had a higher median age at CRC diagnosis as has been previously reported in the literature (Katz et al., 2013; Phatak et al., 2013). A lower percentage of tumors in the proximal colon and a higher percentage of tumors in the rectum were observed among Hispanics (PRH and USH). Similarly, in a study analyzing racial/ethnic disparities in CRC survival in a cohort of 13,958 patients from 6 healthcare systems associated with the Cancer Research Network diagnosed with incident CRC during 1993-1998, a higher percentage of rectal tumors (37%) and lower percentage of proximal tumors (34%) were observed in USH compared to NHB and NHW (Doubeni et al., 2007). The percentage of incident CRC observed in the rectum and proximal colon in PRH (29% and 35%, respectively) and the USH (32% and 37%, respectively) were comparable to the percentages reported in the abovementioned study.

When comparing stage at diagnosis, PRH had the lowest percentage of tumors diagnosed at localized stages, the highest percentage of tumors diagnosed at regional, and the lowest percentage at distant stages compared to USH, NHB, and NHW. The reduced number of cases diagnosed at distant stages in PRH may be due to the fact that more than twice the number of cases in PRH had an unknown stage of diagnosis compared to the other racial/ethnic groups. Even though the number of cases diagnosed at unknown stages was high, the reduced number of cases diagnosed at local stages and increased number of cases diagnosed at regional stages may be explained by the low adherence with CRC screening among PRH (Fecal occult blood test and sigmoidoscopy/colonoscopy) compared to individuals in the US during 1997-2010 (Lopez-Charneco et al., 2013). In terms of tumor differentiation, a higher percentage of well differentiated tumors (23.7%) and a lower percentage of poorly differentiated tumors (6.3%) were observed in PRH compared to the other racial/ethnic groups. Poorly differentiated metastatic adenocarcinomas are associated to worse survival compared to tumors with well-differentiated histology (Golan, Urban, Berger, & Lawrence, 2013).

Disparities in relative survival rates for CRC in PRH were observed according to gender. When combining both sexes, PRH and USH relative survival rates were comparable. This similarity and the higher 1-, 3-, and 5-year relative survival rates among Hispanics compared to NHB may be in part due to the fact that a higher percentage of tumors in the rectum compared to NHB, which had the highest percentage of proximal tumors. Individuals with regional tumors (stage II and III) in the rectum have been reported to higher overall survival rates than individuals with tumors in the colon (Joern et al., 2015). In addition, tumors located in the rectum more commonly present with symptoms as compared to tumors localized in the proximal colon, thus an earlier diagnosis and treatment is expected. Although NHW and NHB have similar distribution of cases according to location, additional factors, including differences in socioeconomic status and access to treatment, have been reported to contribute to the consistently reported low survival rates among NHB compared to other racial/ethnic groups (Gomez, O'Malley, Stroup, Shema, & Satiriano, 2007; White, Vernon, Franzini, & Du, 2010). Overall, higher survival rates were observed in females compared to males in all racial/ethnic groups. Surprisingly, PRH females had higher survival rates than USH. However, PRH males had lower survival rates than NHW and USH. Furthermore, PRH were the only racial/ethnic group in which a more marked survival advantage was observed among females (66.0%) compared to males (60.3%). In a population-based study evaluating racial/ethnic differences in CRC survival in 41,901 individuals diagnosed between 1992 and 1996, decreased survival among USH males compared to females was observed and was attributed to males being diagnosed at more advanced stages (Gomez et al., 2007; White et al., 2010).

Survival disparities according to age were observed among the racial/ethnic groups studied. When comparing 5-year relative survival among individuals 50-59 years old, PRH, USH, and NHB had comparable survival rates, which were markedly lower than NHW. However, a marked lower 5-year relative survival was observed in NHB < 60 years whereas the survival rates in PRH, USH, and NHW were comparable. The higher survival rates observed among Hispanics (USH and PRH) in individuals ≥ 60 years compared to individuals 50-59 years old

could be in part due to Medicare health insurance coverage in this age group compared to the younger cohort.

When comparing 5-year relative survival for CRC according to stage at diagnosis, survival disparities were observed among the racial/ethnic groups studied. PRH (85%) and NHB (83%) had the *lowest* survival in individuals diagnosed at localized stages. Our data revealed that both groups had the highest percentage of individuals that did not undergo treatment, which might explain this survival disparity. Since the number of individuals diagnosed at localized stages was similar between PRH, USH, and NHB, the observed survival disparities in PRH and NHB are most likely not due to screening, but in access to treatment. Results from a small study examining CRC outcomes in PR in a private practice setting support that CRC survival disparities among PRH are influenced by access to proper healthcare (Echenique, 2008). PRH had the *lowest* survival rates in regional cancers. PRH had the highest percentage of individuals that did not undergo treatment, which may explain the high mortality observed in this group. The fact PRH have a greater percentage of rectal tumors and well-differentiated tumors, both associated with a better prognosis compared to colon malignancies and poorly differentiated tumors, suggest that other factors, such as type of medical insurance coverage, access to healthcare, and socioeconomic factors may be contributing to the high mortality among PRH with regional disease. In a study evaluating the effects of type of insurance coverage on CRC survival in PR on patients diagnosed during 2004-2005, a higher percentage of individuals with the government health plan compared to non-government health plans were diagnosed with advanced CRC. Individuals with the government health plan had significantly lower 3- and 5-year survival compared to CRC patients with non-government health plans supporting that this survival disparity is due to access to healthcare (Ortiz-Ortiz, Ramirez-García, Cruz-Correa, Rios-Gonzalez, & Ortiz, 2014). PRH had the highest survival in distant stages. However, this estimate may not be accurate due to the low percentage of distant tumors in this cohort (10%) and the high percentage of tumors with unknown staging (13%) compared to the other racial/ethnic groups studied which had > 18% and < 5.7%, respectively. Analysis of CRC relative risk of death by race/ethnicity showed that PRH had a significantly *higher relative risk of death* from CRC compared to NHW. Moreover, PRH and NHB had 30% higher risk of death as compared to NHW. Noted disparities in CRC screening and access to healthcare have been extensively documented among NHB (Laiyemo et al., 2010; Tammana & Laiyemo, 2014) (Centers for Disease Control and Prevention (CDC), 2012) and PRH (LI Echenique, 2008; Ortiz-Ortiz et al., 2014).

A limitation in this study is that in the PRH cohort the number of cases with unknown tumor stage was higher compared to the other racial/ethnic groups studied, which could affect the precision of the observed survival estimates among PRH. Future analyses are needed to determine if indeed PRH have a higher survival or if this data is an artifact due to the large number of unstaged tumors in this cohort. In addition, the study design did not allow the evaluation of other key factors such as comorbidities (e.g. obesity), lifestyle (e.g. smoking) and socioeconomic factors including insurance status, which are strongly associated with survival. Other possible limitations could be race/ethnicity classification errors, staging errors, errors in death certificates or lack of life tables. Nevertheless, the results of this investigation provide new data on cancer disparities among PRH a Hispanic subpopulation in which CRC is the leading cause of cancer death.

In summary, this study provides valuable CRC outcomes data according to sex and stage of diagnosis in a population with high CRC mortality. The disparities in relative survival rates for CRC observed in PRH according to sex and stage at diagnosis warrant further investigation. Furthermore, the comparisons between racial/ethnic groups in the US shows a marked survival disparity and a relative risk of death similar to NHB, the racial/ethnic group with worse survival in the US (Surveillance, Epidemiology, and End Results (SEER) Program 2012). Since CRC disparities among NHB have been extensively studied, this information may shed light on the factors contributing to the decreased survival in PRH. Health policy directed at increasing population based CRC screening, eliminating barriers to diagnosis, and treatment are of outmost importance to decrease the burden of this disease among Hispanics subpopulations. Furthermore, the racial/ethnic CRC survival disparities observed support CRC disparities among Hispanics subgroups and warrant further investigation of CRC determinants and risk factors affecting these populations.

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