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The Effect of Race/Ethnicity on the Age of Colon Cancer Diagnosis

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ABSTRACT

BACKGROUND: Colorectal cancer is the third most commonly diagnosed cancer in the United States. Notably, racial/ethnic disparities exist in both incidence and mortality. **PURPOSE**: The aim of this case study was to investigate the impact of race/ethnicity on age at diagnosis of colorectal cancer in a defined population in Suffolk County, NY. **METHODS**: Data were retrospectively collected on race/ethnicity, health insurance status, age at diagnosis, stage at diagnosis, gender, smoking status, alcohol intake, tumor location, and body mass index for colorectal cancer patients with medical records in the Stony Brook University Medical Center database (2005-2011). Population-based data on Hispanic and non-Hispanic Whites were obtained from the Surveillance, Epidemiology, and End Results registry of New York State for an overlapping time period. Permutation-based ANCOVA and logistic regression with stepwise variable selection were conducted to identify covariates and first-order interactions associated with younger age at diagnosis and cancer stage as a dependent categorical variable.

RESULTS: Of 328 colorectal cancer patients, Hispanics were diagnosed at a median younger age of 57y vs. 67y than non-Hispanic Whites (FDR = 0.001). Twenty-six percent of Hispanics were diagnosed with colorectal cancer prior to the recommended age (50y) for colorectal cancer surveillance compared to 11% of non-Hispanic Whites (FDR =0.007). Analysis of New York State registry data corroborated our findings that Hispanic colorectal cancer patients were diagnosed at a median younger age than non-Hispanic Whites. Permutation-based ANCOVA identified race/ethnicity and health insurance as significantly associated with age of diagnosis (P=0.001). Logistic regression selected (younger) age at diagnosis as being significantly associated with stage IV disease. The limitations of the case study reside in the use of self-reporting of race and ethnicity and in the small sample sizes.

CONCLUSIONS: Hispanics may be at higher risk for colorectal cancer (<50>y) and younger age at diagnosis is associated with advanced disease.

Keywords: age, ethnicity, race, colorectal cancer, Hispanic, permutation based ANCOVA

INTRODUCTION

In the United States, racial disparities with respect to colorectal cancer (CRC) incidence and mortality have been reported in patients of African descent compared with those of Caucasian descent.[1-3] In contrast, the age-adjusted CRC incidence is reported to be lower in Hispanics than in non-Hispanic Whites.[2] The impact of race/ethnicity on CRC incidence could be due to differences in genetic backgrounds and environmental factors, such as diet and smoking, as well as to differences in access to and utilization of health care services.[4-19] Although the incidence and mortality rates for colorectal cancer have been declining over the past 30 years, recent publications have reported an increased incidence of CRC in patients under the age of 50, which is the recommended age for initiating colonoscopic surveillance.[20-23] These observations have prompted discussions on individualizing the timing of initial screening based on race/ethnicity.[24,25]

Here we report our investigation into the impact of race/ethnicity on the age of CRC diagnosis using retrospective data (2005-2011) obtained from the pathology database at the Stony Brook University Medical Center. These results were compared with population-based data collected during an overlapping four-year period (2004-2007) by the Surveillance, Epidemiology, and End Results (SEER) New York State registries. Overall, the aim of this case study was to investigate whether race and ethnicity have an impact on age at diagnosis of CRC in a geographically defined population.

MATERIALS AND METHODS

Study design: A retrospective case study of colorectal cancer was conducted using data obtained by searching the pathology database at the Stony Brook University Medical Center over six years (2005-2011). Population-based data collected by the SEER New York State registries (2004-2007) were used for comparison only.

Subjects: Retrospective study. This case study was approved by the Stony Brook University Institutional Review Board. A search was conducted using an existing electronic surgical pathology database (CoPath). The demographic data with respect to age, race/ethnicity, and health insurance were obtained by review of the electronic medical records. The covariates were entered into the Stony Brook Digestive Disease Research database after stripping the data of all identifying information and assigning each subject a study code. Race and ethnicity were defined in accordance with the federal standards set by the U.S. Census (http://www.whitehouse.gov/omb/fedreg_race-ethnicity). Following those standards, race/ethnicity was self-declared and/or based on the primary language declared (e.g. Spanish) and categorized as non-Hispanic White, Hispanic White, non–Hispanic Black, Asian, Native American, or Unknown/Other. To isolate the effects of Hispanic ethnicity, Hispanics who were also Black or Asian were classified as Black and Asian, respectively. Eleven of the thirty-seven Hispanic subjects included in the analysis were of unknown race; the race of all other subjects was known. Native American (n=1) and Asian (n=9) patients were excluded from analysis due to extremely low numbers. Covariates. Smoking status was classified as current smoker, non-smoker, or ex-smoker (stopped smoking for at least a year). Alcohol consumption was classified as either never/past/occasional or current weekly/daily. Medical insurance was classified as self-pay (no health insurance), Medicaid (Medicaid, Medicaid equivalent, and CHAMPUS/Tricare) or private (private and Medicare/Private). CRC location was classified as right-sided (tumors located at or proximal to the splenic flexure), left-sided (sigmoid, descending colon) or rectal. For staging, CRC stages 0-III were grouped together as non-metastatic. CRC stage IV

represented metastatic disease based on the TNM/AJCC staging system and review of the medical, surgical, pathologic and radiologic records.[22]

Population-based data for comparison. De-identified population-based data recorded in the New York State SEER database for years 2004 through 2007 was obtained for CRC patients (after excluding patients diagnosed with appendiceal and anal cancers). The data were analyzed for patients in two categories: non-Hispanic Whites and Hispanic Whites.

Statistical analysis: Comparisons between minority racial/ethnic groups and non-Hispanic Whites were carried out using the Kruskal Wallis test for continuous variables and the chi-square test for categorical variables. To address the multiple comparison issue, we applied the Benjamini-Hochberg method to adjust P-values to the false discovery rate (FDR). [26] Effect of covariates on age of diagnosis. The effect of race/ethnicity, gender, smoking, alcohol, body mass index (BMI), health insurance, tumor location, cancer stage, and all first-order interactions on the age of diagnosis as the dependent continuous variable was further analyzed by permutation-based ANCOVA with stepwise variable selection and a threshold significance of 0.05.[24] Effect of selected covariates on tumor stage. The effect of race/ethnicity, gender, smoking, alcohol, BMI, health insurance, tumor location, and age as a categorical variable (<50 vs. ≥50) on the tumor stage as the dependent categorical variable (Stage 0-III vs. IV) was further analyzed by logistic regression with stepwise variable selection and a threshold significance of 0.05.

RESULTS

Clinical and Economic Features of CRC Patients: Identification of subjects for analysis. The electronic surgical pathology records of 382 CRC patients were identified in the Stony Brook University database from the selected years of our retrospective study, 2005 through 2011. These records were examined for the presence of complete data for all of the covariates to be evaluated. As a result, 37 CRC cases were excluded due to incomplete data on cancer staging (resections were performed elsewhere), and 17 patients were excluded due to missing data for alcohol and smoking status. Of the remaining 328 CRC subjects identified by retrospective review of existing records, 265 (80%) were non-Hispanic White, 37 (11%) were Hispanic, 17 (5%) were Black, and 9 (3%) were Asian. Because of the low number of Asian patients, further comparisons focused on non-Hispanic Whites, Hispanics, and Blacks (n = 319, see Table 1). Analyses were carried out using the Kruskal Wallis test for continuous variables and the chi-square test for categorical variables. The multiple comparison issue was addressed as described in Materials and Methods. Initial analysis - age. As presented in Table 1, the median age of the Hispanic patients was lower than that of the non-Hispanic White patients (57 y vs. 67 y, P = 0.0003, FDR = 0.002). The median age of Blacks was also lower than that of non-Hispanic White patients but did not reach statistical significance. A larger proportion of Hispanic than non-Hispanic White colorectal cancer patients were diagnosed prior to reaching the recommended age (50y) for initiating surveillance colonoscopies (P=0.002, FDR = 0.007). Initial analysis – other covariates. A larger proportion of minority patients (Hispanic and non-Hispanic Black) than non-Hispanic White patients had Medicaid insurance. Because smoking, heavy alcohol use, and obesity are associated with a higher risk of CRC, we compared the three groups with respect to smoking, alcohol use, and BMI. No significant differences were found. We also found no significant differences with tumor location or tumor stage between the three racial/ethnic groups.

Age of Diagnosis is Related to Race and Economic Status: The effects of race/ethnicity and the other covariates (listed in Table 1) on the age of colorectal cancer diagnosis (as a continuous variable) were further analyzed by permutational ANCOVA with

stepwise variable selection (see Materials and Methods). As shown in Table 2, race and ethnicity was selected as significantly associated with age of diagnosis in the final model. Additional parameters/factors selected were the type of health insurance, smoking status, tumor stage, tumor location, and first-order interactions between smoking and tumor location and between smoking and tumor stage. Private (including Medicare patients with secondary private) insurance was associated with older age of diagnosis. Stage IV and left-sided tumor location were associated with younger age of diagnosis.

Table 1. Clinical characteristics of non-Hispanic White, Hispanic and Black colorectal cancer patients.

	White Non-Hispanic (n=265)	**Hispanic (n=37)**	**Black Non-Hispanic (n=17)**	**P-value**	**FDR**
Median Age (Range)	67 y (23-93)	57 y (38-80)	58 y (41-83)	**0.0003**	**0.001**
Age <50 (%)	11%	26 %	22%	**0.002**	**0.007**
Male (%)	48%	58%	72%	0.123	0.221
Smoking (%)				0.267	0.176
Current	36%	33%	18%		
Ex-smoker	21%	22%	12%		
Never smoked	43%	45%	70%		
Alcohol (%)				0.222	0.333
Not Current/Rare	81%	92%	88%		
Weekly/Daily	19%	8%	12%		
Median BMI (Range)	27 kg/m^2 (13-53)	27 kg/m^2 (16.2-36)	25 kg/m^2 (18-37)	0.649	0.649
Insurance (%)				**<0.0001**	**<0.0001**
Self-pay	2%	11%	6%		
Medicaid	9%	42%	50%		
Medicare	9%	5%	6%		
Private	80%	42%	38%		
Tumor Location (%)				0.298	0.383
Right colon	44%	47%	72%		
Left colon	40%	37%	17%		
Rectum	16%	16%	11%		
Tumor Stage (%)				0.615	0.649
Stage 0-III	71%	71%	83%		
Stage IV	29%	29%	17%		

To address multiple comparison issues, the Benjamini-Hochberg method was applied to adjust P-values to the false discovery rate (FDR). The variables and first order interactions with FDR $\leq$ 0.05 are bolded.

Analysis of New York State SEER population-based data collected from 2004 through 2007 revealed that of 38,202 non-Hispanic White CRC patients, 2525 (7%) were diagnosed under the age of 50, which is the recommended age for initiating colonoscopic surveillance. Of 3,452 Hispanics (White only), 470 (14%) were diagnosed prior to the age of 50. Of 7,047 Blacks (non-Hispanic and Hispanic), 825 (12%) were diagnosed under the age of 50. Thus, a higher proportion of Black and Hispanic patients were diagnosed prior to age 50 ($P < 0.0001$). However, the age-adjusted incidence rate, calculated based on the 2000 Census data, was increased in the Black but not in the Hispanic CRC patients.

Table 2. Permutation-based ANCOVA with stepwise variable selection results for age of diagnosis.

		R^2	P value	FDR
Main effects	Insurance	0.075	<0.0001	<0.0001
	Smoking	0.055	<0.0001	0.0003
	Tumor Location	0.032	0.0004	0.001
	Race	0.016	0.030	0.042
	Tumor Stage	0.010	0.045	0.045
Interactions	Smoking * Tumor Stage	0.020	0.013	0.024
	Smoking * Tumor Location	0.026	0.040	0.045

The variables and first order interactions are listed below. To address multiple comparison issues, the Benjamini-Hochberg method was applied to adjust P-values to the FDR. The variables and first order interactions with FDR ≤ 0.05 are bolded.

Race and Age of Diagnosis are Associated with Metastatic Staging: To further examine the relationship between the threshold age of initiating surveillance colonoscopy and tumor stage, we reanalyzed the data using tumor stage as the dependent variable (see Table 3). As shown in Table 3, age of diagnosis <50y was associated with metastatic stage IV disease. Therefore, since these patients would not be eligible for initiation of surveillance colonoscopy for asymptomatic disease under the current guidelines, we inferred that colorectal cancer patients diagnosed prior to age 50 undergo diagnostic colonoscopy for symptomatic and consequently more advanced disease.

Table 3. Logistic regression with stepwise variable selection results for metastatic Stage IV disease at diagnosis.

		P value	FDR
Main effects	BMI	0.231	0.672
	Alcohol (weekly/daily)	0.012	0.062
	Age of diagnosis (<50y)	**0.001**	**0.005**
	Gender (female)	0.254	0.672
Interactions	BMI * Alcohol (weekly/daily)	0.010	0.062
	Alcohol (weekly/daily) * Gender (female)	0.016	0.063

The variables and first order interactions are listed below. To address multiple comparison issues, the Benjamini-Hochberg method was applied to adjust P-values to the FDR. The variables and first order interactions with FDR ≤ 0.05 are bolded.

DISCUSSION

In this case study we examined the effect of race/ethnicity on the age of colorectal cancer diagnosis at a single tertiary center in Suffolk County, NY over a six-year period (2005-2011). The largest race/ethnic minority in this case study was the Hispanic population. We observed that Hispanic patients were diagnosed at a younger median age than non-Hispanic Whites and that a larger proportion of Hispanic patients were diagnosed prior to the age of 50. This fact held true even when the eleven Hispanic subjects of unknown race were excluded from the analysis (data not shown). A difference between Blacks and non-Hispanic Whites was observed but was

not significant. However, this lack of statistical significance may have been due to the limitations of being underpowered. Local patterns of physician referrals to this tertiary referral center potentially introduced selection bias with respect to the demographics of the CRC patients at this institution. Furthermore, the small number of minority patients in this case study placed constraints on our overall conclusions. The sample size number was outside of our control and was due in great part to the racial demographics associated with Stony Brook, NY and patients entering Stony Brook University (SBU) Medical Center. However, comparative analysis of the New York SEER population-based dataset collected over roughly the same time period confirmed that a higher proportion of Hispanic than non-Hispanic White CRC patients (14% vs. 7%, $P < 0.0001$) were diagnosed prior to reaching the age of 50 years. Two previous studies, one conducted in New York City and another in San Antonio, TX, noted that the mean age of Hispanic colorectal cancer patients was lower than that of non-Hispanic Whites.[6,7] Although not specifically addressed in the published report of SEER data[3], analysis of patients who underwent curative resection for CRC in seven other geographic areas further confirmed that a higher proportion of Hispanics than non-Hispanic Whites (12% vs. 9%, $P < 0.0001$) are more likely to be diagnosed with CRC prior to reaching the age of 50 years.[4]

These results appear incongruous with the lower estimated age-adjusted incidence of CRC in Hispanics compared to non-Hispanic Whites. One explanation is that the overall Hispanic population is younger than the non-Hispanic White population in the United States. In support of this explanation, it should be emphasized that the age-adjusted incidence rate is calculated based on a projection of the 2000 Census demographic data. The Hispanic population represents the fastest growing ethnic minority; as of July 2009 it became the largest ethnic minority, representing 16% of the US population.[27] Notably, Suffolk County had the largest Hispanic population increase in the state of New York over the past decade (http://somosnewyork.org/2011/06/22/2011-interesting-census-facts/). In addition, migration of large numbers of undocumented Hispanic immigrants from Central America over the past decade could make it difficult to accurately estimate the age-adjusted incidence rate in the Hispanic population, particularly for the younger age groups.

The time period covered by this case study overlapped with the Suffolk County Preventive Endoscopy Project (Project SCOPE),[23] which recruited 800 indigent patients aged 50 or above to undergo surveillance colonoscopy at SBU Medical Center. Project SCOPE was designed to serve as a feasibility model for providing screening for average-risk, uninsured or under-insured individuals. Any patient with a cancer detected through Project SCOPE in the years 2005-2009 was included in the 382 patients but was not flagged, since at the time we were not cross-referencing the cancer patient list with the SCOPE patient list. Sixty-nine percent of the patients screened through Project SCOPE were minorities, of which 45% were Hispanic. Because of the high proportion of minorities, Project SCOPE addressed and may have introduced an approach that serves to ameliorate racial/ethnic disparities associated with access to surveillance colonoscopy.

It has been noted that the incidence of early onset CRC is increasing. Earlier colonoscopic surveillance of first-degree relatives of probands with early-onset CRC is currently recommended by the American Cancer Society. Racial/ethnic differences in age-adjusted incidence of CRC raise questions as to whether lowering the recommended threshold age for initiating colonoscopic surveillance should be individualized based on factors such as race/ethnicity. For example, the American College of Gastroenterology has recommended that the threshold age be lowered from 50y to 45y in Blacks, where the estimated incidence of CRC

is higher. However, simply lowering the age for Hispanics is problematic, since the age-adjusted incidence rate is estimated to be lower in Hispanic compared with non-Hispanic White or Black populations in the U.S. Also, the Hispanic population is extremely heterogeneous. Prospective collection of more detailed demographic data (e.g. country of origin if foreign born) and potentially confounding covariates is clearly needed to further delineate the genetic and/or environmental factor(s) that contribute to potential racial/ethnic differences in early-onset CRC.

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