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REVIEW

Disparities in colorectal cancer in African-Americans *vs* Whites: Before and after diagnosis

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Abstract

There are differences between African-American and white patients with colorectal cancer, concerning their characteristics before and after diagnosis. Whites are more likely to adhere to screening guidelines. This is also the case among people with positive family history. Colorectal cancer is more frequent in Blacks. Studies have shown that that since 1985, colon cancer rates have dipped 20% to 25% for Whites, while rates have gone up for African-American men and stayed the same for African-American women. Overall, African-Americans are 38% to 43% more likely to die from colon cancer than are Whites. Furthermore, it seems that there is an African-American predominance in right-sited tumors. African Americans tend to be diagnosed at a later stage, to suffer from better differentiated tumors, and to have worse prognosis when compared with Whites. Moreover, less black patients receive adjuvant chemotherapy for resectable colorectal cancer or radiation therapy for rectal cancer. Caucasians seem to respond better to standard chemotherapy regimens than African-Americans. Concerning toxicity, it appears that patients of African-American descent are more likely to develop 5-FU toxicity than Whites, possibly because of their different dihydropyridine dehydrogenase status. Last but not least, screening surveillance seems to be higher among white than among black long-term colorectal cancer survivors. Socioeconomic and educational status account for most of these differences whereas little evidence exists for a genetic contribution in racial disparity. Understanding the nature of racial differences in colorectal cancer allows tailoring of screening and treatment interventions.

Key words: African-American; Caucasian; Chemotherapy; Colorectal cancer; Dihydropyrimidine dehydrogenase; 5-FU; Irinotecan; Oxaliplatin; Socioeconomic; Stage

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INTRODUCTION

Colorectal cancer is the third most common malignancy and third most frequent cause of cancer-related death in the United States, with 148 810 new cases and 49 960 deaths anticipated in 2008[1]. Screening for this type of malignancy reduces mortality through detection of cancer at an earlier, more treatable stage as well as by identification and removal of the precursor lesion, the adenomatous polyp. Today there is a range of options for colorectal cancer screening in the average-risk population, with current technology falling into 2 general categories: stool tests, which include tests for occult blood or exfoliated DNA, and structural exams, which include flexible sigmoidoscopy, colonoscopy, double-contrast barium enema, and computed tomographic colonography. Several treatment options are available after diagnosis depending on the stage including radiation for rectal cancer, surgery and systemic chemotherapy for colon and rectal cancer.

This is a review of the bibliography concerning the differences between African Americans and Caucasians before and after the diagnosis of colorectal cancer. Issues such as screening trends, biologic background, racial variation of colorectal cancer risk and sub site specific risk, prognosis, treatment and surveillance are examined. In addition, socioeconomic and educational disparity has been taken into consideration.

RACIAL DIFFERENCES BEFORE DIAGNOSIS

Colorectal screening disparities between African American and White populations

Being African American is associated with a lower screening rate for colorectal cancer[2-12]. Perceived positive beliefs or barriers about colorectal cancer screening, physician recommendation and knowledge of screening tests and colorectal cancer risk are responsible for a great deal of the difference. Socioeconomic status which is composed of education and income also account partly for the observed difference. African Americans and Caucasians seem to prefer different screening options. In addition, screening disparity exists among Blacks and Whites with positive family history. However, not all studies confirm these data.

Knowledge about colorectal cancer and screening: African-Americans' perceptions of sigmoidoscopy and colonoscopy differ from fecal occult blood testing (FOBT) with respect to perceived benefits *vs* barriers. Specifically, barriers are significantly and negatively associated with FOBT and sigmoidoscopy, whereas there is a significant positive association between perceived benefits and sigmoidoscopy or colonoscopy but not with FOBT[13]. Higher educational status and greater knowledge of flexible sigmoidoscopy predicted greater adherence to screening flexible sigmoidoscopy guidelines, whereas greater knowledge of FOBT and doctor recommendation predicted greater adherence to FOBT screening guidelines in an African American population in East Harlem[14]. Knowledge status about colorectal cancer is lower in African Americans than in Whites[15]. In addition, African Americans who adhered to the screening guidelines tended to be more knowledgeable about colorectal cancer and to hold more positive beliefs about the benefits of screening than those who were not up-to-date with screening. Moreover, they tended to receive more physician recommendation and to have better insurance status[16]. Low-income African Americans are optimistic and hopeful about early colorectal cancer detection and believe that thorough and accurate screening is valuable. Lack of colorectal cancer knowledge and fear are major barriers to screening for this population[17]. African American descent, communication with the health care provider[18], knowledge about colorectal cancer[18] and physician recommendation[19] predicts adherence to the screening guidelines. Perceived absolute risk, comparative risk or colorectal cancer concerns, predict planning to get an FOBT in the next 2 years among low income African Americans[20]. It appears that doctor's recommendation, awareness of screening, older age, greater education and perceived susceptibility account for the differences in colorectal cancer screening among Blacks and Whites in a study[11]. African American women who perceive fewer barriers, more benefits, and have increased confidence in the accuracy of screening are more likely to undergo screening[21].

Socioeconomic contribution to the racial screening disparity: Having either a screening sigmoidoscopy or colonoscopy is positively associated with educational status, being married, higher household income, recent medical visit, higher age and public or private insurance among African Americans[5]. White race and higher socioeconomic status are associated with higher rate of physician recommendation of screening[6]. A study showed that screening rate varies less by race than by region[22]. This study concentrated on Southern US regions where there are high concentrations of African Americans as well as high levels of unemployment and poverty. Screening disparities between Blacks and Whites were eliminated after adjusting for socioeconomic status as this was defined by income and education[23]. Medicare coverage of colonoscopy since 2001 did reduce racial screening disparities between elderly Whites and Blacks[24].

Blacks and Whites undergo different screening tests: It appears that preferred screening techniques vary according to race. African Americans tend to receive significantly less frequent screening colonoscopy than Whites. On the other hand, African Americans are more likely to receive a screening sigmoidoscopy at regular intervals[5]. Whites are more likely, in a statistically significant manner, to undergo an endoscopy as a colorectal cancer screening test than African Americans[9]. Racial/ethnic minorities are significantly less likely than Whites to prefer computed tomography colonography (CTC) over optical colonoscopy (OC) (Whites, 65.7%; Blacks, 45.1%; Hispanics, 35.8%; and other, 35.7%; $P < 0.001$). Racial/ethnic minorities are less satisfied with CTC (Whites, 8.4 ± 1.7; Blacks, 7.8 ± 1.7; Hispanics, 7.4 ± 1.8; and other, 7.5 ± 2.1; $P = 0.001$) and are significantly less willing to undergo CTC again in the future (Whites, 95.5%; Blacks, 80.3%; Hispanics, 84.9%; and other, 85.7%; $P = 0.006$)[25]. Among tests that examine the entire colon, barium enema is more commonly used among Blacks, whereas colonoscopy is more commonly among Whites[26].

Screening among people with positive family history: Screening for colorectal cancer differs between Blacks and Whites with a positive family history for colorectal cancer. Among people with multiple affected first degree relatives (FDRs), or relatives diagnosed before age 50 years, African Americans were less likely than Whites to follow the screening guidelines after adjusting for age, sex, educational status, annual income, insurance status, total number of affected and unaffected FDRs, and time since last medical visit. Specifically, 27.3% of the African-Americans reported having had a colonoscopy during the last five years *vs* 43.1% of Whites [$P < 0.001$, odds ratio (OR) = 0.51, 95% CI 0.38-0.68][27]. Another study confirmed this

outcome (27.9% of Whites *vs* 9.3% of Blacks with a positive family history had undergone an endoscopic screening procedure in the last 10 years, $P = 0.03$). After adjusting for age, family history, gender, educational level, insurance status, and usual source of care, Whites were more likely to be current with early initiation endoscopic screening recommendations than African Americans (OR = 1.38, 95% CI 1.01-1.87)[28]. Family history did not predict screening in African Americans when the analysis was controlled for age, education, and insurance. African Americans who have a family history are less likely to screen compared with their white counterparts and compared with African Americans who are at average risk for colorectal cancer ($P < 0.05$)[29]. Tailored intervention increased screening *via* FOBT in a statistically significant manner in the Caucasian but not in the non-Caucasian population of first degree relatives of people affected with colorectal cancer[30].

Studies that do not confirm higher screening rates in the White population *vs* Blacks: Few studies have shown either a higher screening rate in the African-American than in the white population, or no racial difference. In a Veteran medical centre, patients' files were retrospectively analyzed and it was shown that Blacks are more likely to receive either an FOBT within the last year or a flexible sigmoidoscopy/colonoscopy within the last five years than their white counterparts although physician recommendation did not vary among the racial groups[31]. No screening differences were noticed between African Americans, European Americans and Native Americans[32]. Adherence to the Medicare-covered intervals for colorectal cancer screening tests is low (56.8% for Whites, 39.1% for African Americans), and did not significantly differ by race after adjustment. African Americans were, however, significantly less likely to have ever been tested (OR = 0.48, 95% CI 0.33-0.70) and more likely to have had an endoscopic test than an FOBT in this study (OR = 3.06, 95% CI 1.70-5.51)[33]. After adjusting for age, having a regular doctor and participation in general medical exams, Blacks and Whites did not vary significantly in their current colorectal cancer screening status, with an OR of 1.1 (95% CI 0.7-1.6)[34]. No racial difference was observed in the percentage of people with a positive FOBT who underwent a colonoscopy in the following 12 mo[35]. A study among low income women showed that African-American descent predicts a lower likelihood of reporting having had screening colonoscopy within the past 10 years (OR = 0.46, $P < 0.001$) although following the screening guidelines did not vary by race[36].

Findings from colonoscopy screenings: A study[37] carried out and led by David Lieberman, MD, of Portland VA Medical Center collected information from colonoscopy screenings of 5464 African-Americans and 80 061 Whites from 67 screening centers around the United States as published in the September 24, 2008 issue of *The Journal of the American Medical Association*. The researchers found that "asymptomatic black men and women undergoing colonoscopy screening are more likely to have one or more polyps sized more than 9 mm compared with white individuals. The differences were especially striking among women. These findings emphasize the importance of encouraging all black men and women to be screened."

The findings: Nearly 8% of African-American patients had one or more polyps larger than 9 mm; 6% of Whites had one or more polyps larger than 9 mm; African-American women had a 62% greater risk of having such a polyp in the colon when compared with white women; African-American men had a 16% greater chance of having large polyps when compared with white men.

Sub site location of colorectal cancer according to race

It appears that colon cancer sub site varies according to race. Differences in location among African-Americans and non-Hispanic Whites implicate different screening guidelines in the two racial groups.

A study showed that the proportion of sigmoid colon cancer is 15.6%-21.3% lower in African Americans than non Hispanic Whites over three successive time periods between 1973 and 2002, whereas the diagnosis of descending colon cancer is 40.5%-45.3% higher in the African-American than the white subgroup[38]. Regression analysis in this study confirmed that tumors sited proximal to the sigmoid colon or to the splenic flexure are more common in Blacks than in Whites. African Americans are less likely to have colonic polyps (OR = 0.77, 95% CI 0.70-0.84) and more likely to have colonic tumors than Whites (OR = 1.78, 95% CI 1.14-2.77), but they are more likely to have polyps in the proximal colon (OR = 1.30, 95% CI 1.11-1.52) and colonic tumors in the proximal colon (OR = 4.37, 95% CI 1.16-16.42)[39]. Advanced proximal colon cancer is more frequent in African-Americans[40-42]. Blacks are more likely to receive a diagnosis of proximal colon cancer than distal colorectal cancer but within the same sub site, they are less likely than Whites to receive a diagnosis of localized disease[41]. African Americans tend to have more proximal tumors than Whites[43]. Another study confirmed African American predominance in proximal colorectal cancer and white predominance in distal tumors[44]. Carcinoma in situ has the same pattern of distribution in Blacks and Whites as invasive colorectal carcinoma (white predominance in distal disease and black predominance in proximal disease)[45].

However, an older study, showed no racial variation in cecum or ascending colon cancer incidence, black predominance in transverse or descending colon cancer and white predominance in sigmoid and rectal cancer[46].

Racial variation of colorectal cancer risk

African-Americans are at increased risk of developing colon cancer[47], especially distant disease[48], compared with Whites, but rectal cancer rate was shown to be higher among Whites when compared with Blacks[47]. Black seniors are less likely to be diagnosed with early

stage disease than their white counterparts and this association is greater in areas with high racial segregation and low income[49]. Between the years 1992-2001 a decline is observed in colorectal cancer incidence among Whites (1.2% per year in white men and 0.7% per year in white women) but not among Blacks[50]. Colorectal cancer was found to be more common in the black population than in the other racial groups and colorectal cancer screening beginning at the age of 50 is more cost-effective in the black population[51]. Colorectal cancer incidence was higher in the white than the black race until the mid 1980s whereas the opposite is true in the following years. Furthermore, the same study showed that proximal and transverse colon cancers are more common in Blacks than in Whites and distal colon and rectal cancer are more common in Whites than in Blacks. Colorectal cancer is of lower grade and of greater stage in Blacks than in Whites. In both racial groups, there is a decline in the incidence of distant disease, more in Whites than in Blacks. In the former, the incidence of localized and regional disease was found to be increasing, whereas in the latter this incidence is decreasing[42]. Colorectal cancer risk in people younger than 50 years old is higher in African Americans than in Whites[52]. In addition, the high incidence and younger age at presentation of colorectal cancer in African Americans warrants initiation of colorectal cancer screening at the age 45 year rather than 50 year[53].

Nutritional habits and colorectal cancer risk: African-Americans were found to consume less micronutrients than Whites. High intake of beta carotene, vitamin C and calcium are associated with a lower risk of colorectal cancer in the white population whereas high intake of vitamin C and E are inversely associated with colorectal cancer risk in the African-American population[54]. Usage of non-steroidal anti-inflammatory drugs is associated with a reduced risk of colorectal cancer and this association did not vary among African Americans and Whites[55]. Fiber consumption is significantly associated with 50%-60% reduced risk of colorectal cancer in African Americans and non-significantly with 30% reduced risk of colorectal cancer in Whites[56]. Hydrogen response to 10 g of oral lactulose is significantly higher in the African-American than in the Caucasian American population implicating a difference in colonic bacterial metabolism between the two groups[57]. African Americans in all age groups seem to consume fewer mean daily servings of total dairy, milk, cheese, and yogurt than non-African Americans, and have lower mean intakes of calcium, magnesium, and phosphorus[58].

Racial polymorphism variation: Cigarette smoking was found to be positively associated with colorectal cancer risk in the white but not in the black population[59]. This study also examined the possible association between GSTM1 and GSTT1 polymorphisms with colon cancer. There is a trend towards increased risk of colon cancer for individuals with GSTM1 null (African Americans, OR = 1.43, 95% CI 0.98-2.09; Whites, OR = 1.19, 95% CI 0.90-1.58) and a decreased risk of colon cancer for individuals with GSTT1 null (African Americans, OR = 0.59, 95% CI 0.40-0.86; Whites, OR = 0.72, 95% CI 0.53-1.00). There are weak interactions between GSTT1 null and cigarette smoking in Whites, and GSTM1 null genotype and cigarette smoking in African Americans. African Americans are more likely to have the BLFA haplotype of the vitamin D receptor (6.5% in the white population *vs* 41.2% in the African American population) which was found to be associated with increased risk of colorectal cancer (OR = 2.4, 95% CI 1.38-4.38)[60]. Adjusted ORs for the combined effects of codon 677 CC and codon 1298 AA genotypes (these codons being part of the 5-10 methylenetetrahydrofolate reductase gene) and folate intake < 400 μg/d are 1.9 (95% CI 1.1-3.4) in African Americans and 2.5 (95% CI 1.2-5.2) in Whites[61]. Arachidonate lipoxygenase (ALOX) and cyclooxygenase (COX) are considered important in the development of colon cancer. ALOX5 Glu254Lys, COX2 C-645T and Val511Ala allele frequencies vary among Caucasians and African-American controls ($P < 0.001$). The ALOX5-1752 and -1699 polymorphisms are in linkage disequilibrium ($P < 0.001$) and lower colon cancer risk in Caucasians in ALOX5 haplotype analyses ($P = 0.03$). Furthermore, an inverse association is observed between A alleles at positions -1752 and -1699 of ALOX5 and colon cancer risk in Caucasians, but not in African-Americans. Caucasians with A alleles at ALOX5-1752 have a reduced odds of colon cancer *vs* those with G alleles [OR (GA *vs* GG) = 0.63, 95% CI 0.39-1.01; OR (AA *vs* GG) = 0.33, 95% CI 0.07-1.65, P (trend) = 0.02]. The same is observed for ALOX5 G-1699A [OR (GA *vs* GG) = 0.59, 95% CI 0.37-0.94; OR (AA *vs* GG) = 0.27, 95% CI 0.06-1.32, P (trend) = 0.01][62]. Serum 25-(OH)D levels are higher in non-Hispanic Caucasians than in subjects of other ethnicities ($P < 0.001$) in both people with and without colorectal adenomas. Serum 25-(OH)D is inversely associated with colorectal adenomas showing a 26% decrease in the rate of colorectal adenoma with each 10 ng/mL increase in serum 25-(OH)D[63]. N acetyltransferase 2 rapid/intermediate genotype is associated with increased colon cancer risk in Whites (OR = 1.4, 95% CI 1.0-1.8), when compared with the slow genotype, which is not true for Blacks[64]. N-myc downstream-regulated gene 1 (NDRG1) expression is correlated to histopathological type, Dukes' stage and HIF-1 alpha expression in US-Caucasian patients but not in US-African American patients. Interestingly, Kaplan-Meier survival analysis demonstrated that NDRG1 expression correlated significantly with poorer survival in US-African American patients but not in other patient groups[65].

POSTDIAGNOSIS DISPARITIES BETWEEN WHITES AND AFRICAN AMERICANS

Racial prognosis difference due to socioeconomic status, stage and other tumour characteristics

Colorectal cancer mortality declined in Whites but

increased in Blacks from 1950 to 1992[66]. However, mortality has declined in both Blacks and Whites from 1990 to 1998, although the rate for Blacks has remained high[67]. Disparity in survival between Blacks and Whites is confirmed by another study[68]. There is no difference in survival between Blacks and Whites with colorectal cancer among patients with the same stage receiving the same treatment[69]. Recurrence-free survival is modestly lower in African-Americans than in Whites with operable rectal cancer [hazard ratio (HR) 1.25, 95% CI 0.94-1.66] whereas racial disparity in mortality rate is larger (HR 1.45, 95% CI 1.09-1.93)[70]. Furthermore, after adjusting for socioeconomic status, mortality in stage Ⅱ and Ⅲ colon cancer patients was only marginally higher in African Americans than in Whites[71]. An older study showed that among patients with colon cancer, black to white mortality was 1.5 (95% CI 1.2-1.9) and 1.2 after adjustment for stage (95% CI 1.0-1.5)[72]. In the same study, differences in mortality was observed in stages Ⅱ and Ⅲ (HR 1.8, 95% CI 1.0-3.1 and HR 1.5, 95% CI 1.2-2.3, respectively) but not in stage Ⅳ. Furthermore, another study confirmed that Blacks are more likely to die from colorectal cancer than Whites (relative risk = 1.34, 95% CI 1.26-1.42)[73]. In this study, socioeconomic status and stage accounted for half of the disparity for all stages and socioeconomic status accounted for all the disparity in stage Ⅲ of colon and stage Ⅱ and Ⅲ of rectal cancer. In addition, co-morbidity did not contribute to the disparity, but treatment (surgery, radiation, chemotherapy) explained a very small proportion of the black-white difference. The fully-adjusted relative mortality rate comparing Blacks to Whites was 1.14 (1.09-1.20) for all-cause mortality and 1.21 (1.14-1.29) for colorectal cancer specific mortality. A large meta-analysis (including articles in English from 1966 to August 2007) showed that racial disparities in survival for colon cancer between African-Americans and Caucasians are only marginally significant after adjusting for socioeconomic factors and treatment (HR 1.13, 95% CI 1.01-1.28)[74]. On the other hand, another study showed that there is higher stage-specific mortality in Blacks compared with Whites and socioeconomic status accounts for some but not all of this disparity[75]. Increased mortality rate in Blacks compared with Whites is the outcome of another study[76]. After adjustment for age, sex, histology, site within the colon, and stage, African Americans are more likely to die compared with Caucasian patients with colorectal cancer (colon: HR 1.19, 95% CI 1.14-1.25; rectum: HR 1.27, 95% CI 1.17-1.38). However, after further adjustment for socioeconomic status and treatment, the risk of death for African-Americans compared with Caucasians is substantially diminished (colon: HR 1.08, 95% CI 1.03-1.13; rectum: HR 1.11, 95% CI 1.02-1.20)[77]. Survival in patients suffering from colorectal cancer with more than 16 years of education increased from 1993 to 2001 [2.4% ($P < 0.001$), 4.8% ($P = 0.011$), 3.0% ($P < 0.001$), and 2.6% ($P = 0.030$) annually among white men, black men, white women, and black women, respectively]. Among patients with less than 16 years of education, an increase in mortality was observed only in black men (2.7% per year; $P < 0.001$) whereas the death rate remained stable in the other groups[78]. Blacks with colonic adenocarcinoma were found to have a reduced 5- (OR = 1.67, 95% CI 1.21-2.33) and 10- (OR = 1.52, 95% CI 1.12-2.07) year survival than Whites after surgery[79]. The strongest and statistically significant association was observed only among patients with stage Ⅱ. No racial differences in overall survival were observed among patients with rectal cancer. In this study no neo-adjuvant or adjuvant treatment was given to the patients. Among patients who underwent an operation for primary colorectal carcinoma and did not receive pre-surgical or post-surgical chemotherapy, 54% of African Americans and 21% of Caucasians with high grade tumors died within the first year after surgery ($P = 0.007$). African Americans with high-grade tumors were 3 times (HR 3.05, 95% CI 1.32-7.05) more likely to die of colon carcinoma within 5 years post-surgery, compared with Caucasians with high-grade tumors. There were no survival differences by race among patients with low-grade tumors[80].

Another study showed no association between socioeconomic status and survival in patients with colorectal cancer treated in city and university hospitals[81]. However, Blacks are more likely to be treated in city than in university hospitals (53% *vs* 20.6%, $P < 0.001$). Patients treated in city hospitals had a worse prognosis than those treated in university hospitals and Blacks had a worse prognosis in both city and university hospitals in this study.

Racial variation in treatment

In adjusted comparisons with white patients with colorectal carcinoma, African American patients reported more problems with coordination of care ($P < 0.001$), psychosocial care ($P = 0.03$), access to care ($P = 0.03$), and health information ($P < 0.001$)[82].

Surgical treatment of colorectal cancer in African-Americans and Whites: Among patients who underwent surgery for rectal cancer, the rate of sphincter-ablating procedure was 37% for Whites and 43% for Blacks [adjusted odds ratio (AOR) 1.42, 95% CI 1.23-1.65][83]. Blacks had a higher risk of dying from colorectal cancer (HR 1.17, 95% CI 1.06-1.30) in a study and adjustment for tumour stage reduced the hazard ratio to 1.11 and surgical treatment further reduced hazard ratio to 1.06[84]. Black patients were more likely than Whites not to receive surgical treatment in stage Ⅰ (OR = 2.08, 95% CI 1.41-3.03 among males; OR = 2.38, 95% CI 1.69-3.45 among females) and Ⅳ (OR = 1.25, 95% CI 1.01-1.56 among males; OR = 1.41, 95% CI 1.14-1.72 among females) colon cancer and most stages of rectal cancer, and they were more likely to refuse recommended treatment[85]. Black patients were less likely to undergo surgery than Whites (86% *vs* 91%, $P = 0.02$) but the same study showed no racial differences in overall survival[86]. However, long term survival after rectal cancer surgery was shorter for Blacks

than for Whites [five-year survival rates were 41% and 50%, respectively ($P < 0.0001$)]. In this study, African Americans were more likely to be treated by low volume surgeons and not to receive adjuvant chemotherapy[87].

Chemotherapy and radiation therapy in white and black patients with colorectal cancer: African Americans were treated less frequently with chemotherapy and radiation therapy compared with their Caucasian counterparts, in a retrospective analysis of data coming from a single institution[88]. African Americans with stage Ⅲ colon cancer are less likely to receive adjuvant chemotherapy after surgery and they gain less benefit from adjuvant chemotherapy than Whites[89]. There is no statistically significant difference between black and white patients with stage Ⅱ and Ⅲ rectal carcinoma in the frequency of consultation with a medical oncologist (73.1% for Blacks *vs* 74.9% for Whites, difference = 1.8%, 95% CI 5.9%-9.5%, $P = 0.64$) or radiation oncologist (56.7% *vs* 64.8%, difference = 8.1%, 95% CI 0.5%-16.7%, $P = 0.06$), but Blacks are less likely than Whites to consult with both a medical oncologist and a radiation oncologist (49.2% *vs* 58.8%, difference = 9.6%, 95% CI 0.9%-18.2%, $P = 0.03$). Among patients who visited an oncologist, black patients are less likely than white patients to receive chemotherapy (54.1% *vs* 70.2%, difference = 16.1%, 95% CI 6.0%-26.2%, $P = 0.006$), radiation therapy (73.7% *vs* 83.4%, difference = 9.7%, 95% CI 0.4%-19.8%, $P = 0.06$), or both (60.6% *vs* 76.9%, difference = 16.3%, 95% CI 4.3%-28.3%, $P = 0.008$). Patient and provider characteristics have minimal influence on the racial disparity in the use of adjuvant therapy[90]. The same was shown for stage Ⅲ colon cancer in elderly patients: consultation with a medical oncologist was equal among black and white patients, but the former were less likely to receive chemotherapy (59.3% *vs* 70.4%, difference = 10.9%, 95% CI 5.1%-16.4%, $P < 0.001$). Disparity was higher among patients aged 66-70 (black patients 65.7%, white patients 86.3%, difference = 20.6%, 95% CI 10.7%-30.4%, $P < 0.001$) which was confirmed by regression analysis and decreased in older patients. Disparity in this age group was partially due to patient, physician, hospital and environmental factors (accounted for 50%), surgical length of stay, neighbourhood socioeconomic factors (27%) and health system factors (12%)[91]. Furthermore, 53% of Whites and 56% of Blacks received no radiation therapy for stage Ⅱ to Ⅲ rectal cancer (AOR, 1.30; 95% CI, 1.15-1.47) in a study[83]. White patients received standard adjuvant therapy more frequently than African-Americans (OR = 1.75; 95% CI 1.09-2.83)[92].

On the other hand, race was not associated with receipt of adjuvant chemotherapy in patients with stage Ⅲ colon cancer[93]. This is confirmed by another study in which after adjustment for socioeconomic status, race was not associated with receiving adjuvant treatment or radiation in stage Ⅲ colon and stage Ⅱ, Ⅲ rectal cancer[94].

Racial variation in response to chemotherapy: In at least one study[95], it was shown that Caucasian patients with metastatic colorectal cancer respond better to standard chemotherapy combinations (IFL, FOLFOX or IROX) than African-Americans (response rate for African Americans 30%, for Caucasians 41%, $P = 0.015$). This was shown in multivariate analysis as well (29% response rate for African Americans *vs* 41% for Caucasians, $P = 0.012$). The difference was noted in each treatment arm. However, no association was noted between race and time to progression or overall survival. The same study showed racial variation in pharmacogenomic parameters. Specifically, UGT1A1 6/7 and 7/7 polymorphisms were more common in African Americans, whereas UGT1A1 6/6 was more common in Caucasians ($P = 0.0081$). In addition, ercc2-d A/A and A/B was more common in Caucasians and ercc2-d B/B more common in African Americans ($P = 0.0002$). GSTM1-0 was more frequently absent in Caucasians and more frequently present in African Americans ($P = 0.001$). Finally xrcc1-r399q C/C was more frequent in African Americans than in Caucasians, whereas in the other genotypes the opposite was true ($P = 0.0006$). Moreover, a study showed that there is a higher risk of neutropenia in UGT1A1 7/7 patients especially in patients treated with IROX[96]. No association was found between this genotype and overall survival, time to progression, response rate or diarrhoea. Among previously treated patients with metastatic colorectal cancer who received bevacizumab or FOLFOX4 or the combination of these regimens, African Americans differed significantly from Whites in response rate and overall survival, whereas there was no significant difference in progression-free survival (RR: 10.2% *vs* 11.8%, $P = 0.03$; OS: 10.2 mo *vs* 11.2 mo, $P = 0.03$; PFS 4.2 mo *vs* 5.0 mo)[97].

Table 1 Differences in toxicity of the standard treatments for colorectal cancer between whites and AAs

Regimens	Toxicity
Irinotecan and oxaliplatin	FOLFIRI, FOLFOX and IROX are less toxic to AAs than Whites
Fluoropyrimidines	5-FU is less toxic to AAs than Whites
Cetuximab	Whites are more prone to hypersensitivity reactions

AAs: African Americans.

Disparities in treatment related toxicity between the two ethnic groups: The data concerning toxicity difference between Caucasians and African Americans are summarized in Tables 1 and 2.

Stage and grade at diagnosis

Two studies showed that black patients with colorectal carcinoma are diagnosed at a more advanced stage than their white counterparts[76,77]. Blacks are more likely to be diagnosed at a younger age and at a more advanced stage than white patients with rectal cancer[83].

Apart from socioeconomic status, black-white

Table 2 Differences in toxicity of the standard treatments for colorectal cancer between Whites and African Americans

Regimens	Toxicity	Difference	Reference
Irinotecan and oxaliplatin	FOLFIRI, FOLFOX and IROX are less toxic to AAs than Whites	34% *vs* 48%, $P = 0.004$, for severe toxicity 5% *vs* 17%, $P = 0.004$ for diarrhea	[95]
Fluoropyrimidines	5-FU regimens in the adjuvant setting differed between AA and Whites, with AA experiencing statistically significantly lower rates	Diarrhea ($P < 0.001$) Nausea ($P < 0.001$) Vomiting ($P = 0.01$) Stomatitis ($P < 0.001$) Overall toxicity ($P = 0.005$)	[98]
DPD deficiency	AA, particularly AA women, have significantly reduced DPD enzyme activity compared with Whites, which may predispose this population to less 5-FU toxicity	-	[99]
Cetuximab	In a retrospective analysis, it was shown race was strongly associated with HSR to cetuximab among patients with CRC and head and neck cancer, with Whites experiencing HSR more frequently than AA	(Fisher exact) $P = 0.017$	[100]

HSR: Hypersensitivity reactions; AA: African American.

differences in tumour grade among patients with colon cancer were found. Specifically, Blacks appeared less likely to suffer from poorly differentiated tumors-grade 3 (OR = 0.44; 95% CI 0.22-0.88) with lymphoid reaction (OR = 0.49; 95% CI 0.26-0.90) when compared with Whites. This outcome remained statistically significant after adjusting for age, sex, metropolitan area, socioeconomic status, body mass index, and health care access and utilization. A trend without statistical significance was shown towards less high-grade (grade 3) nuclear atypia, mitotic activity, and tubule formation in Blacks compared with Whites. These findings were confirmed in patients with advanced but not with early disease. In addition, no differences were found in blood and lymphatic vessel invasion, mucinous histology, necrosis or fibrosis.

Blacks were more likely to suffer from better differentiated tumors in the proximal, but not in the distal colon. These outcomes suggest that factors other than tumour differentiation contribute to the different survival between Blacks and Whites along with socioeconomic status disparity[101]. Another study confirmed that African Americans are more likely to be diagnosed with more advanced and better differentiated tumors than Whites[43].

African-Americans were more likely to present with life-threatening symptoms at the time they were diagnosed with colorectal cancer than Whites. This association was found to be independent of socioeconomic status. In addition, African Americans were more likely to die during their hospitalization when compared to Whites in both overall and high socioeconomic status[102].

Quality of life in long term colon cancer survivors

African Americans are more likely to report better quality of life and psychological well being (marginally statistically significant, $P = 0.07$) as long-term colon cancer survivors[103]. Among colon cancer survivors, African Americans presented with higher fruit/vegetable consumption than Whites[104]. White colorectal cancer survivors are more likely to undergo colon examination surveillance than African Americans 1, 2 and 5 years after diagnosis[105]. After adjusting for socio-demographic, hospital and clinical characteristics, Blacks are 25% less likely than Whites to receive surveillance[106]. This finding was not statistically significant in another study (relative risk 0.70, $P = 0.14$)[107].

CONCLUSION

African Americans are at increased risk of developing advanced colorectal cancer and are less likely to be up to date with colorectal cancer screening guidelines when compared with Whites. They also tend to be diagnosed with more proximal, more advanced and better differentiated tumors than Whites. In addition, they seem to have a worse prognosis and to receive appropriate treatment to a lesser extent. Socioeconomic factors, educational status, different beliefs and physician recommendation account for most of the disparity. However, little evidence exists concerning genetic differences which would explain the variety in colorectal cancer predisposition, sensitivity to carcinogens, response and toxicity of treatment between Blacks and Whites. In our opinion further research on these issues should be performed. Therefore, continued research efforts are necessary to disentangle the clinical, social, biological, and environmental factors that constitute this racial disparity. In addition, results across data sources should be considered when evaluating racial differences in cancer outcomes.

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