Published in final edited form as:
Cancer. 2009 December 15; 115(24): 5798–5806. doi:10.1002/cncr.24598.

Effect of Comorbidity and Body Mass Index on Colon Cancer Survival of African American and Caucasian Patients

Robert B. Hines, MPH[1], **Chandrakumar Shanmugam, MD**[2], **John W. Waterbor, MD, DrPH**[1], **Gerald McGwin Jr., MS, PhD**[1], **Ellen Funkhouser, DrPH**[1,3], **Christopher S. Coffey, PhD**[4], **James Posey, MD**[5], and **Upender Manne, MS, PhD**[2,6]

[1]Department of Epidemiology, University of Alabama at Birmingham, Birmingham, Alabama

[2]Department of Pathology, University of Alabama at Birmingham, Birmingham, Alabama

[3]Department of Preventive Medicine, University of Alabama at Birmingham, Birmingham, Alabama

[4]Department of Biostatistics, University of Alabama at Birmingham, Birmingham, Alabama

[5]Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama

Abstract

Background—There is a survival disparity between African Americans and Caucasians with colon cancer. The aims of this study were to quantify the impact of comorbidity and body mass index (BMI) on survival and to assess whether these two variables account for the decreased survival among African Americans.

Methods—Data from patients (n = 496) who underwent surgery for first primary colon cancer at the University of Alabama at Birmingham Hospital from 1981-2002 were analyzed. Hazard ratios (HR) with 95% confidence intervals (CI) were obtained by Cox proportional hazards modeling for the association of race, comorbidity, BMI, and covariates with mortality. The confounding influence of comorbidity and BMI for the increased risk of death associated with African American race was evaluated. Effect modification by tumor stage for the association of comorbidity and BMI with mortality was also assessed.

Results—African Americans experienced an increased risk of death compared to Caucasians (HR=1.34; 95% CI, 1.06-1.68). The highest comorbidity burden was associated with an increased risk of all-cause mortality (HR=1.63; 95% CI, 1.24-2.15). For BMI, being underweight increased the risk of death (HR=1.54; 95% CI, 0.96-2.45), but being overweight/obese was protective (HR=0.77; 95% CI, 0.61-0.97). The effect of comorbidity was seen among those with early stage tumors while the effect of BMI was confined to patients with advanced tumors.

Conclusions—Although comorbidity and BMI impact post-surgery survival of colon cancer patients, they are not the contributing factors for the decreased survival observed among African Americans.

Keywords

Race; Comorbidity; Body Mass Index; Colon Cancer; Survival

[6]Author for correspondence: Upender Manne, MS, PhD Associate Professor, Department of Pathology University of Alabama at Birmingham Kracke Building K515 B, 1922 7th Avenue South Birmingham, AL 35294-7331 Phone: (205) 934-4276; Fax: (205) 975-7284 manne@uab.edu .

Financial Disclosure: There are no financial disclosures from any authors.

Background

In 2008, there were an estimated 108,000 new cases of colon cancer and 50,000 deaths due to colorectal cancer (CRC), which ranks this cancer third in terms of incidence and mortality among men and women in the United States.1 The public health impact of colon cancer has declined over the past 25 years, as evidenced by a decreasing incidence and better survival due to early detection and improved treatment.2 Despite these improvements, there continues to be a survival disparity among non-Hispanic African Americans and non-Hispanic Caucasians.3, 4 For nearly all cancers, including colon cancer, the survival rate of African Americans is less than that of Caucasians.1 In fact, the survival difference between African Americans and Caucasians has increased since the mid-1970s.1 A variety of reasons have been postulated for the survival disparity between the races. Investigators have suggested that differences between African Americans and Caucasians in access to health-care, exposure to risk factors (e.g., obesity), stage at diagnosis, comorbidity, the physician-patient relationship, socioeconomic status, and tumor characteristics may explain the observed racial difference in survival.5–7 The degree to which these factors operate in determining survival, however, remains unknown.

Comorbidity is defined as the presence of other diseases in conjunction with an index disease (e.g., colon cancer) of primary interest.8 Comorbid conditions in the cancer patient impact the timing of cancer detection, treatment, prognosis, and outcome.9 As others have speculated, comorbidity may be partly responsible for the decreased survival observed in African Americans with colon cancer.6 Since comorbid conditions exert their effects at multiple levels along the spectrum of care for the cancer patient, failure to account for comorbidity in cancer studies could result in a confounding bias.10 Thus, it is important to assess whether the increased risk of death in African Americans with colon cancer is due, at least in part, to failure to account for comorbid conditions in statistical analyses.

The association between obesity and the risk of developing colon cancer has been the subject of numerous epidemiologic investigations.11 The consensus on this issue is that obesity increases the risk of developing colon cancer, though the evidence is stronger for men than women.12 Despite the many studies that have focused on obesity and incident colon cancer, few have assessed the impact of body habitus and the relationship with survival following a diagnosis. In addition, no study has investigated the role of BMI in the decreased survival observed among African Americans with colon cancer compared to Caucasians. Differences in body habitus between African Americans and Caucasians could shed light on the issue of survival disparity between the races.

The aims of the present study were to assess the role of comorbidity and body habitus with survival following surgery for colon cancer in a patient population collected from one institution. In addition, we sought to investigate the potential confounding influence of comorbidity and BMI as an explanation for the decreased survival of non-Hispanic African Americans with colon cancer relative to non-Hispanic Caucasians. Further, we examined the impact of comorbidity and BMI by tumor stage in order to increase understanding of how these risk factors determine survival according to tumor stage. The results of this study will contribute to a greater understanding of the role of comorbidity and BMI and the association with survival following surgery for colon cancer in general and also will allow insight into the survival disparity typically observed between African Americans and Caucasians with colon cancer.

Materials and Methods

Our study population consisted of patients who underwent surgery for sporadic (non-hereditary/familial) adenocarcinoma of the colon at The University of Alabama at Birmingham (UAB) Hospital from 1981-2002. The termination date for the accrual of follow-up information was June 1, 2008. The initial patient population was comprised of 631 participants. In order for patients to be eligible for this study, the diagnosis of first primary sporadic colon cancer had to be the earliest diagnosis of any cancer in the patient (with the exception of non-melanoma skin cancer). Therefore, patients previously diagnosed with other types of cancer or colon cancer (n = 63) were excluded. Also excluded were subjects with multiple primary tumors (n = 13) and those with unknown tumor grade (n = 3). As an aim of this study was to assess the effect of comorbidity on survival, and as the impact of comorbidity increases with age, patients who were less than 40 years of age (n = 22) were excluded. By excluding patients less than 40, the probability of the tumor arising in individuals with a family or genetic history of CRC was minimized.13 By excluding subjects who survived less than one month after tumor resection (n = 21), those who died of complications following surgery were removed from the study population. Also excluded were patients who were originally from other countries (n = 7). Finally, since BMI was a primary variable of interest in this study, six participants with missing height information were excluded. After the above exclusions were made, the study sample consisted of 496 patients. This study was approved by the Institutional Review Board (IRB) at UAB.

Tumor specific characteristics were obtained from pathology reports and adjudicated by two of the authors (CS, UM). Tumors were classified by the tumor-node-metastasis (TNM) system and staged according to the American Joint Committee on Cancer (AJCC) system as Stages I, II, III, or IV.14 Tumor grade was recorded as well differentiated, moderately differentiated, poorly differentiated, or unknown (no tumors were graded as undifferentiated), and the tumor grade was ascertained by a pathologist (CS). As suggested by Compton et al.,15 well and moderately differentiated tumors were referred to as “low grade,” and poorly differentiated tumors were designated as “high grade.” The presence of bowel obstruction at the time of surgery and whether the participant received blood transfusions during surgery was also recorded.

Demographic, clinical, and patient information regarding age at time of surgery, gender, race (self-identified), surgery date, insurance status, comorbidity, height and weight, smoking status, information on therapy, and perioperative variables was obtained from medical records. Age was treated as a continuous variable. Year of surgery was categorized in four 5-6 year intervals based on the distribution of patients from 1981-2002. Smoking information was recorded as current, former, or never smoked. Insurance status was recorded as whether or not the patient had private insurance coverage. Information pertaining to adjuvant chemotherapy was ascertained, and a dichotomized variable for receipt of any chemotherapeutic regimen was created. For each participant, height and weight information at the time of surgery were obtained. In addition, whether or not the patient experienced weight loss prior to the diagnosis of colon cancer was recorded. From the height and weight data, BMI $\left[BMI = \frac{\text{weight} \quad (kg)}{\text{height} \quad (m)^2}\right]$ was calculated, and each participant was categorized as underweight (BMI < 18.5), normal weight (BMI: 18.5–24.9), overweight (BMI 25.0–29.9), or obese (BMI ≥ 30.0), according to WHO and NIH recommended guidelines.16, 17

Comorbidity information was abstracted by the primary author (RH) from the medical records up to the date of surgery. These data were obtained from sources in the medical records, including physician notes, anesthesia notes, nursing notes, and discharge

summaries. Only comorbidities present before surgery were included in the comorbidity assessment. The Adult Comorbidity Evaluation-27 (ACE-27) was used as the instrument of comorbidity assessment in this study, as it was designed to assess the comorbidity burden specifically in patients with cancer.18 With the ACE-27, each study participant was given an overall grade of none, mild, moderate, or severe comorbidity as detailed by Piccirillo et al. 18 Since having a previous cancer was an exclusion criterion for this study, information pertaining to cancer was not used in the calculation of comorbidity burden.

Follow-up data on each patient were obtained from the UAB Tumor Registry. This information was updated by the UAB Tumor Registry, every 6 months for each patient by contacting the patient or a family member. If a patient had died since the last follow-up contact, the date of death was recorded, though cause of death was not obtained. Patients that were alive at the termination date of the study were right censored at the last contact date. If a patient was recorded as alive, and ≥ 3 years had elapsed since the last contact, the patient was designated as “lost to follow-up.”

Statistical Analysis

Survival time was calculated from the date of surgery until either death, the termination date of the study, or the last date of contact for patients who were still alive. The event of interest was death from any cause. All reported *P* values were two-sided, and statistical significance was defined as $P < 0.05$.

Chi-square (χ^2) statistics for categorical variables and t-tests for continuous variables were used to assess differences in vital status, demographic variables, comorbidity, tumor characteristics, chemotherapy status, and perioperative variables according to race. The Kaplan-Meier method was used to compare the survival experience of African Americans and Caucasians, with statistical significance determined by the log-rank test. The Cox proportional hazards (PH) model was used to obtain bivariate and adjusted hazard ratios (HR) with 95% confidence intervals (CI) for the association of risk factors and other covariates with mortality. From the bivariate analyses, each variable that obtained $P < 0.20$ was considered a potential confounder for the risk factors of interest in this study (race, comorbidity, BMI) and the association with all-cause mortality. For the multivariable model, potential confounders that met these criteria were included in a model containing age, tumor stage, race, comorbidity, and BMI. The final model was obtained by step-wise removal (the variable with the highest *P* value was removed and the model reanalyzed) of covariates that were no longer associated with mortality and, therefore, were not confounders. By testing the interaction between each variable with time, the proportional hazards assumption was evaluated and met for race, comorbidity, and BMI in the multivariable model. In addition, the statistical significance of all two-way interactions between African American race, comorbidity, body habitus, and tumor stage was assessed. From the multivariable model, the confounding influence of comorbidity and BMI for the association of African American race with survival was evaluated. Finally, effect modification of comorbidity and BMI was assessed by tumor stage.

Results

Characteristics of the study population by race are shown in Table 1. The proportion of African Americans (39.2%) and Caucasians (60.8%) represents a natural proportion of all colon cancer patients who underwent surgery at UAB Hospital. Significantly more African Americans had died at the end of follow-up (74.1% v. 62.7%; $P < 0.01$). The median time of death for African Americans was more than two years earlier (49.5 v. 76.1 months; $P = 0.06$) than that for Caucasians. There were more African American females (62.2 v. 49.8%; $P < 0.01$), but the gender distribution among Caucasians was uniform. Relative to

Caucasians, more African Americans enrolled during the earlier years of the study period (1981-1991: 41.4 % v. 30.4%; $P = 0.03$). African Americans were also less likely to have private insurance (46.6% v. 81.1%; $P < 0.01$) and more likely to be non-smokers (66.3% v. 55.8%; $P = 0.04$). At the time of surgery, there was no difference in the mean age of African American and Caucasian study participants.

Regarding comorbidity, African Americans were more likely to be in the severe category of comorbidity (22.8% v. 13.9%; $P < 0.01$) (Table 1). For BMI, proportionately more African Americans were underweight (8.3% v. 2.6%) and obese (28.5% v. 16.5%; $P < 0.01$) compared to Caucasians. There was no difference between the races with regard to tumor stage at the time of surgery ($P = 0.08$), though African Americans were less likely to have high-grade tumors (14.5% v. 23.1%; $P = 0.02$). African Americans were also less likely to have received adjuvant chemotherapy (18.7% v. 32.3%; $P < 0.01$). There was no difference by race in participants who presented with bowel obstruction, received blood during surgery, or reported recent weight loss prior to surgery (Table 1).

The association of risk factors with death in the multivariable model is shown in Table 2. Based on the results obtained from the unadjusted association of each risk factor with survival, categories were combined when the hazard ratios were similar. Therefore, strata for comorbidity, BMI, and tumor stage were combined. From the results obtained in the multivariable model, African Americans experienced a 34% increased risk of death, which was statistically significant (HR= 1.34; 95% CI, 1.06-1.68). In addition, comparison of the adjusted and crude hazard ratios revealed negative confounding; the risk of death associated with African American race became stronger in magnitude and statistically significant after adjustment for other risk factors. For comorbidity, only those with the most severe burden had an increased risk of death. Study participants with severe comorbidity at the time of surgery had a 63% increased risk of death due to any cause (HR= 1.63; 95% CI, 1.24-2.15).

In the assessment of body habitus at the time of surgery (Table 2), underweight patients were at increased risk of death (HR= 1.54; 95% CI, 0.96-2.45), which was marginally statistically significant; overweight/obese participants had a decreased risk (HR= 0.77; 95% CI, 0.61-0.97). The likelihood ratio test was performed for the overall effect of BMI with death due to any cause. The addition of BMI significantly improved the survival model (χ^2_2=20.4; $P < 0.01$). Stage was highly predictive of death. Compared to those with stage I or II (early stage) cancers, those with stage III disease experienced nearly a 2-fold increased risk of death (HR= 1.95; 95% CI, 1.50-2.45), and those with stage IV tumors had nearly a 9-fold increase in risk (HR= 8.96; 95% CI, 6.60-12.18). High tumor grade was associated with a 55% increased risk (HR= 1.55; 95% CI, 1.19-2.03), and the presence of bowel obstruction increased the risk of death by 51% (HR= 1.51; 95% CI, 1.19-1.91). In the unadjusted analysis, year of surgery (1981-86 v. 1987-2002: HR = 1.42; 95% CI, 1.09-1.85), lack of private insurance (HR= 1.26; 95% CI, 1.01-1.58), receipt of chemotherapy (HR= 1.72; 95% CI, 1.36-2.16), receipt of blood during surgery (HR= 1.95; 95% CI, 1.25-3.03), and recent weight loss (HR= 1.52; 95% CI, 1.22-1.90) were all associated with mortality. None of these covariates, however, remained statistically significant in the multivariable model. Further, no interaction terms were statistically significant.

Table 3 displays the association of African American race with death in five models: the crude association, a model adjusted for stage only, a model adjusted for all risk factors other than comorbidity, a model adjusted for all risk factors other than BMI, and the fully adjusted model. The purpose of this analysis was to evaluate the confounding influence of stage, comorbidity, and BMI in the association of African American race with survival. Comparing the HR obtained for the crude association of African American race with death and the other HRs shown in the table, only stage was a confounder of the race relationship. The possibility

of confounding by comorbidity and/or BMI was assessed by comparing the HRs obtained for the fully adjusted models without these variables shown in the two columns of Table 3 to the fully adjusted HR depicted in the last column. If a substantial shift toward the null for the HR associated with African American race occurred after adjustment for either of these variables, the conclusion was that one or both of these variables did, in fact, explain some of the excess risk of death associated with African American race. That is, failure to account for the confounding influence of comorbidity and/or BMI in previous studies explained a portion of the increased risk of death for African Americans. Nevertheless, after adjustment for either comorbidity or BMI, there was no meaningful change in the HR associated with African American race. The conclusion was that neither comorbidity nor BMI was a confounder of the association of race with death and, thus, that comorbidity and BMI did not explain the increased risk of all-cause mortality observed for African Americans.

The assessment of effect modification by tumor stage for the association of comorbidity and BMI is shown in Table 4. For comorbidity, comparing the ratio measures obtained for early stages to those for advanced stages illustrated the greater impact of comorbidity for those with less advanced disease. In addition, both moderate and severe comorbidity were associated with an increased risk of death for those with less advanced tumors. For early stages of disease, moderate comorbidity increased the risk of death by 74% (HR= 1.74; 95% CI, 1.14-2.65); those with severe comorbidity had a greater than 2-fold increased risk (HR= 2.22; 95% CI, 1.44-3.43). For patients with stage III tumors, comorbidity was not associated with survival. Concerning participants with stage IV colon cancer, there was an increased risk of death associated with moderate and severe comorbidity, though this was not statistically significant. For BMI, there was no association with death for those with early stage tumors. The possibility of detecting a statistically significant association between underweight and death was limited due to small numbers. Nonetheless, there was an association for those with stage III tumors. Being underweight was associated with an 87% increased risk of death compared to normal weight individuals (HR= 1.87; 95% CI, 0.95-3.69). The protective effect of being overweight/obese was confined to those with distant metastatic disease (stage IV); being overweight/obese decreased the risk of death by 42% compared to those of normal weight (HR= 0.58; 95% CI, 0.37-0.90).

Discussion

For patients with colon cancer, various reasons have been put forth to explain the increased mortality of African Americans relative to Caucasians. The goals of this study were to quantify the overall effect of comorbidity and BMI on survival among a population of colon cancer patients, to determine whether the decreased survival among African Americans relative to Caucasians is due to the confounding influence of comorbidity and/or BMI, and to assess effect modification for the impact of comorbidity and BMI by tumor stage. In the present study, those with the highest comorbidity burden had an increased risk of death from any cause. The prognostic impact of comorbidity was confined to those with stage I or II tumors. Further, being underweight was associated with an increased risk of death for those with stage III disease, and being overweight or obese was associated with a decreased risk for those with stage IV disease. Finally, the only confounder for the association of race with death was tumor stage. Adjustment for comorbidity and BMI did not explain the increased mortality for African American patients with colon cancer.

Only the developers of the ACE-27 index have used this index of comorbidity assessment in a population of colon cancer patients.[18, 19] In the study by Piccirillo et al.,[18] increasing comorbidity was associated with decreased overall survival for all digestive system tumors. In the present study, only those with severe comorbidity had an increased risk of death, as shown in other populations of cancer patients,[20] and there was also effect modification by

tumor stage. With increasing stage, the cancer became the primary determinant of survival. This result is consistent with results reported by Read et al19 for colon, breast, and prostate cancer.

Several investigators have adjusted for comorbidity in studies addressing the survival disparity between African Americans relative to Caucasians with colon or colorectal cancer.[21, 22] Though these studies demonstrated an increased risk of death for African Americans after adjustment for comorbidity, they did not address the question of whether comorbidity accounted for any of the excess risk. This question was addressed by Mayberry et al.4 as part of the National Cancer Institute Black/White Cancer Survival Study. These authors found an increased risk of death due to colon cancer and all causes for African Americans relative to Caucasians, although the latter was not statistically significant. After adjustment for stage, the increased risk of colon cancer-specific death associated with African American race decreased by 60%. The addition of comorbidity did not result in a further reduction of the hazard ratio associated with African Americans. However, it is unclear how comorbidity was defined in this study.

According to Mayberry et al.,4 stage is the primary determinant of survival differences by race.5 In our results, however, stage was actually a negative confounder of the association with African American race. This result can be explained by the fact that, though there were no statistically significant differences in stage at diagnosis between African Americans and Caucasians in our study, considerably more Caucasians (22.3% v. 16.8) were diagnosed with distant metastatic disease. This could account for the increase in magnitude of association for African American race that became statistically significant after adjustment for tumor stage.

Only one other study by Gomez et al.3 has investigated the confounding influence of comorbidity in an attempt to explain the racial differences in survival for patients with colon cancer. Similar to our current findings, these authors found that comorbidity did not account for the increased risk of overall or colon cancer-specific mortality observed for African Americans. The comorbidity index used was the Charlson Comorbidity Index (CCI). Though we used a more comprehensive measure of comorbidity assessment (ACE-27) in the present study, we reached the same conclusions as the previous two studies.[3, 4] That is, comorbidity did not explain any of the increased risk of mortality for African Americans with colon cancer.

The BMI component of this study was added to contribute to the few studies in the literature on this subject, to address the limitations of previous studies, and to assess the possible confounding influence of BMI for the association of African American race with mortality. When viewed in the context of tumor stage, the increased risk for underweight and the decreased risk for overweight/obese participants are biologically plausible and relate to the notion of frailty. Various criteria can be used to identify the frail elderly, including malnutrition and the presence of significant comorbidity.23 In our study, most patients who were underweight were older (mean age: 75.7 years) and had either moderate or severe comorbidity (66.7%). Being underweight can be seen as a marker of decreased biological reserve, and thus decreased capacity to compensate for the physical demands imposed by the cancer. Thus, being overweight/obese can be advantageous for individuals with metastatic disease. Perhaps having extra weight (biological reserve) in this scenario translates to a better capacity to withstand the symptoms associated with a cancer of this advanced stage.

In the context of other reported studies, our findings obtained for BMI are consistent with the increased risk associated with underweight but are at odds with studies that found an increased risk for obese individuals. Meyerhardt et al.24 reported that, among men and

women with stage II or III colon cancer enrolled in a clinical trial, underweight men experienced an increased risk of overall mortality; for women, obesity was associated with an increased risk of death. As part of the National Surgical Adjuvant Breast and Bowel Project (NSABP), Dignam et al.25 reported that, among patients with Dukes B and C colon cancer, underweight participants were at increased risk of non-colon cancer-related deaths and that severely obese participants were at increased risk of death due to colon cancer. To our knowledge, the current study is the first that has investigated body habitus in an effort to explain the increased risk of death for African Americans with colon cancer.

The present study has a number of strengths. Our method of comorbidity assessment, comprehensive medical record review, is superior to other methods of comorbidity assessment, e.g., the use of administrative data.26 Another asset of this study is the long follow-up period of the study population. Each study participant had the potential to be followed for a minimum of over five years from the end of the accrual period to termination of the study.

There are, however, limitations of the current study. One (which could also be an asset) is the 20+ year time period for entry into the study. In an effort to account for improvements in patient care that occurred during this time period, the data were adjusted for year of surgery. Nonetheless, there may be differences in the probability of survival between patients who entered the study in the earlier periods compared to the later years that were not sufficiently accounted for by adjusting for year of surgery. Another weakness is that information on cause of death was not available. This information would have been useful in determining the impact of comorbidity and BMI on cancer-specific as well as non-cancer causes of death.

The issue of racial disparity in survival among patients with cancer is likely multifactorial and has been attributed to various causes. Though the current study has shown that comorbidity and BMI are associated with all-cause mortality in patients with colon cancer, the results presented herein as well as previous investigations suggest that comorbidity and BMI do not likely explain the decreased survival associated with African American race in an academic medical center setting. There is evidence from VA studies, which support the idea that when access to treatment is equivalent, the racial disparity in survival is greatly reduced.21, 22 Whether the survival difference is diminished due to equal access to the medical system or due to similarity of socioeconomic background or other potential confounders among this population, however, is a matter of speculation.27 As socioeconomic and sociodemographic variables are often unavailable or inadequately measured, differences in these and other pathobiologic variables between African Americans and Caucasians may be responsible for observed survival differences by race in colon cancer. Further investigations are needed to gain a greater understanding of this complex issue so that efforts can be directed toward the primary cause of mortality differences by race.

Acknowledgments

This work is supported in part by grants from the National Institute of Health/National Cancer Institute (U54-CA118948 and RO1-CA98932-01) to Dr. U. Manne. Robert B. Hines was supported by an NIH/NCI grant (5-R25-CA47888) as part of the Cancer Prevention and Control Training Program. The work involved in the conception of this manuscript was independent of the funding sources. Also, we thank Donald L. Hill, Ph.D., Division of Preventive Medicine, University of Alabama at Birmingham, for his critical review of this manuscript.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008; 58(2):71–96. [PubMed: 18287387]
2. American Cancer Society. Cancer Facts & Figures 2008. American Cancer Society; 2008.
3. Gomez SL, O'Malley CD, Stroup A, Shema SJ, Satariano WA. Longitudinal, population-based study of racial/ethnic differences in colorectal cancer survival: impact of neighborhood socioeconomic status, treatment and comorbidity. BMC Cancer. 2007; 7:193. [PubMed: 17939875]
4. Mayberry RM, Coates RJ, Hill HA, Click LA, Chen VW, Austin DF, et al. Determinants of black/white differences in colon cancer survival. J Natl Cancer Inst. 1995; 87(22):1686–93. [PubMed: 7473817]
5. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer and race: understanding the differences in outcomes between African Americans and whites. Med Clin North Am. 2005; 89(4):771–93. [PubMed: 15925649]
6. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer model of health disparities: understanding mortality differences in minority populations. J Clin Oncol. 2006; 24(14):2179–87. [PubMed: 16682737]
7. Ward E, Jemal A, Cokkinides V, Singh GK, Cardinez C, Ghafoor A, et al. Cancer disparities by race/ethnicity and socioeconomic status. CA Cancer J Clin. 2004; 54(2):78–93. [PubMed: 15061598]
8. Feinstein AR. The Pre-Therapeutic Classification Of Co-Morbidity In Chronic Disease. J Chronic Dis. 1970; 23:455–68.
9. de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity. a critical review of available methods. J Clin Epidemiol. 2003; 56(3):221–9. [PubMed: 12725876]
10. Extermann M. Measuring comorbidity in older cancer patients. Eur J Cancer. 2000; 36(4):453–71. [PubMed: 10717521]
11. Larsson SC, Wolk A. Obesity and colon and rectal cancer risk: a meta-analysis of prospective studies. Am J Clin Nutr. 2007; 86(3):556–65. [PubMed: 17823417]
12. Giovannucci E. Obesity, gender, and colon cancer. Gut. 2002; 51(2):147. [PubMed: 12117867]
13. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology. 2003; 124(2):544–60. [PubMed: 12557158]
14. Greene, FL.; American Joint Committee on Cancer. American Cancer Society. AJCC cancer staging manual. ed. 6th. Springer-Verlag; New York: 2002.
15. Compton C, Fenoglio-Preiser CM, Pettigrew N, Fielding LP. American Joint Committee on Cancer Prognostic Factors Consensus Conference: Colorectal Working Group. Cancer. 2000; 88(7):1739–57. [PubMed: 10738234]
16. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. National Institutes of Health. Obes Res. 1998; 6(Suppl 2):51S–209S. [PubMed: 9813653]
17. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser. 1995; 854:1–452. [PubMed: 8594834]
18. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr. Prognostic importance of comorbidity in a hospital-based cancer registry. Jama. 2004; 291(20):2441–7. [PubMed: 15161894]
19. Read WL, Tierney RM, Page NC, Costas I, Govindan R, Spitznagel EL, et al. Differential prognostic impact of comorbidity. J Clin Oncol. 2004; 22(15):3099–103. [PubMed: 15284260]
20. Borggreven PA, Kuik DJ, Langendijk JA, Doornaert P, de Bree R, Leemans CR. Severe comorbidity negatively influences prognosis in patients with oral and oropharyngeal cancer after surgical treatment with microvascular reconstruction. Oral Oncol. 2005; 41(4):358–64. [PubMed: 15792607]
21. Dominitz JA, Samsa GP, Landsman P, Provenzale D. Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system. Cancer. 1998; 82(12):2312–20. [PubMed: 9635522]

22. Rabeneck L, Davila JA, Thompson M, El-Serag HB. Surgical volume and long-term survival following surgery for colorectal cancer in the Veterans Affairs Health-Care System. Am J Gastroenterol. 2004; 99(4):668–75. [PubMed: 15089900]

23. Winograd CH, Gerety MB, Chung M, Goldstein MK, Dominguez F Jr. Vallone R. Screening for frailty: criteria and predictors of outcomes. J Am Geriatr Soc. 1991; 39(8):778–84. [PubMed: 1906492]

24. Meyerhardt JA, Catalano PJ, Haller DG, Mayer RJ, Benson AB 3rd, Macdonald JS, et al. Influence of body mass index on outcomes and treatment-related toxicity in patients with colon carcinoma. Cancer. 2003; 98(3):484–95. [PubMed: 12879464]

25. Dignam JJ, Polite BN, Yothers G, Raich P, Colangelo L, O'Connell MJ, et al. Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. J Natl Cancer Inst. 2006; 98(22):1647–54. [PubMed: 17105987]

26. Kieszak SM, Flanders WD, Kosinski AS, Shipp CC, Karp H. A comparison of the Charlson comorbidity index derived from medical record data and administrative billing data. J Clin Epidemiol. 1999; 52(2):137–42. [PubMed: 10201654]

27. Alexander DD, Waterbor J, Hughes T, Funkhouser E, Grizzle W, Manne U. African-American and Caucasian disparities in colorectal cancer mortality and survival by data source: an epidemiologic review. Cancer Biomark. 2007; 3(6):301–13. [PubMed: 18048968]

Table 1

Characteristics of the Study Population

Characteristics	African-American n (%)	Caucasian n (%)	P
	193 (39.2)	303 (60.8)	—
Status			< 0.01
Deceased	143 (74.1)	190 (62.7)	
Median overall survival (in months)	49.5	76.1	0.06
Mean age at surgery (± s.d.)	67.2 (11.8)	66.6 (12.5)	0.60
Sex			< 0.01
Male	73 (37.8)	152 (50.2)	
Female	120 (62.2)	151 (49.8)	
Surgery date			0.03
1981-1986	40 (20.7)	36 (11.9)	
1987-1991	40 (20.7)	56 (18.5)	
1992-1996	50 (25.9)	83 (27.4)	
1997-2002	63 (32.6)	128 (42.2)	
Private insurance			< 0.01
Yes	90 (46.6)	244 (81.1)	
Smoking Status			0.04
Non-smoker	128 (66.3)	169 (55.8)	
Former	35 (18.1)	82 (27.1)	
Current	30 (15.5)	52 (17.2)	
ACE-27 Comorbidity			< 0.01
None	25 (13.0)	73 (24.1)	
Mild	69 (35.8)	115 (38.0)	
Moderate	55 (28.5)	73 (24.1)	
Severe	44 (22.8)	42 (13.9)	
BMI			< 0.01
Underweight	16 (8.3)	8 (2.6)	
Normal	70 (36.3)	129 (42.6)	
Overweight	52 (26.9)	116 (38.3)	
Obese	55 (28.5)	50 (16.5)	
Tumor Stage			0.08
1	34 (17.6)	57 (18.8)	
2	63 (32.6)	106 (35.0)	
3	65 (33.7)	72 (23.8)	
4	31 (16.1)	68 (22.4)	
Tumor grade			0.02
High	28 (14.5)	70 (23.1)	
Low	165 (85.5)	233 (76.9)	
Chemotherapy			< 0.01

Characteristics	African-American n (%)	Caucasian n (%)	P
Yes	36 (18.7)	98 (32.3)	
Obstruction			0.57
Yes	60 (31.1)	87 (28.7)	
Received blood			0.91
Yes	10 (5.2)	15 (5.0)	
Recent weight loss			0.18
Yes	69 (35.8)	91 (30.0)	

Table 2

Bivariate and Adjusted Associations with Death

	Hazard Ratios	
Variable	**Unadjusted (95% CI)**	**Adjusted[1] (95% CI)**
Race		
Caucasian	ref	ref
African American	1.23 (0.99, 1.53)	1.34 (1.06, 1.68)
ACE-27 Comorbidity		
Not severe	ref	ref
Severe	1.62 (1.24, 2.11)	1.63 (1.24, 2.15)
BMI		
Underweight	1.81 (1.15, 2.83)	1.54 (0.96, 2.45)
Normal	ref	ref
Overweight/obese	0.83 (0.66, 1.03)	0.77 (0.61, 0.97)
Tumor stage		
Stages I & II	ref	
Stage III	1.96 (1.51, 2.54)	1.95 (1.50, 2.54)
Stage IV	7.38 (5.55, 9.79)	8.96 (6.60, 12.18)
Tumor grade		
Low	ref	ref
High	1.70 (1.32, 2.20)	1.55 (1.19, 2.03)
Bowel obstruction	1.98 (1.58, 2.48)	1.51 (1.19, 1.91)

95% CI indicates 95% confidence interval.

[1] Adjusted for the variables listed as well as age.

Table 3

The Association of African American Race with All-Cause Mortality

	Hazard Ratios with 95% CI				
Variable	**Unadjusted**	**Adjusted for stage**	**Fully adjusted[1] minus comorbidity**	**Fully adjusted[1] minus BMI**	**Fully adjusted[1]**
Race					
Caucasian	ref	ref	ref	ref	ref
	1.23	1.37	1.36	1.38	1.34
African American	(0.99, 1.53)	(1.10, 1.71)	(1.08, 1.71)	(1.10, 1.73)	(1.06, 1.68)

CI indicates confidence interval

[1]The fully adjusted model is adjusted for age, race, comorbidity, BMI, tumor stage, tumor grade, and bowel obstruction.

Table 4

The Association of Comorbidity and BMI with Death by Tumor Stage

	Stages I & II	Stage III	Stage IV
	HR[1] (95% C.I.)	**HR[1] (95% C.I.)**	**HR[1] (95% C.I.)**
ACE-27 Comorbidity			
None/mild	ref	ref	ref
Moderate	1.74 (1.14, 2.65)	0.99 (0.85, 1.68)	1.25 (0.77, 2.02)
Severe	2.22 (1.44, 3.43)	1.16 (0.78, 1.74)	1.80 (0.87, 3.72)

	Stages I & II	Stage III	Stage IV
	HR[1] (95% C.I.)	**HR[1] (95% C.I.)**	**HR[1] (95% C.I.)**
BMI			
Underweight	1.07 (0.50, 2.27)	1.87 (0.95, 3.69)	1.28 (0.16, 10.04)
Normal	ref	ref	ref
Overweight/obese	0.92 (0.65, 1.30)	0.92 (0.59, 1.45)	0.58 (0.37, 0.90)

HR indicates hazard ratio; CI indicates confidence interval

[1]HRs were adjusted for age, race, comorbidity, BMI, tumor grade, and obstruction