Outcomes Among African-Americans and Caucasians in Colon Cancer Adjuvant Therapy Trials: Findings From the National Surgical Adjuvant Breast and Bowel Project

James J. Dignam, Linda Colangelo, Wei Tian, Judy Jones, Roy Smith, D. Lawrence Wickerham, Norman Wolmark

Background: African-Americans generally have lower survival rates from colon cancer than Caucasian Americans. This disparity has been attributed to many sources, including diagnosis at later disease stage and other unfavorable disease features, inadequate treatment, and socioeconomic factors. The randomized clinical trial setting ensures similarity in disease stage and a uniform treatment plan between blacks and whites. In this study, we evaluated survival and related endpoints for African-American and Caucasian patients with colon cancer participating in randomized clinical trials of the National Surgical Adjuvant Breast and Bowel Project (NSABP) to determine whether outcomes were less favorable for African-Americans. Methods: The study included African-American (n = 663) or Caucasian (n = 5969) patients from five serially conducted, randomized clinical trials of the NSABP. We compared recurrence-free survival, disease-free survival (recurrence, new primary cancer, or death), and survival (death from any cause) between blacks and whites by using statistical modeling to account for differences in patient and disease characteristics between the groups. Statistical tests were two-sided. Results: Dukes' stage and number of positive lymph nodes were remarkably similar between African-American and Caucasian patients in each trial. Over all trials combined, an 8% (95% confidence interval [CI] = −6% to 25%; P = .27) excess risk of colon cancer recurrence that was not statistically significant was observed for blacks. A greater disparity in survival was seen, with blacks experiencing a statistically significant 21% (95% CI = 6%–37%; P = .004) greater risk of death. Treatment efficacy appeared similar between the groups. Conclusions: While the overall survival prognosis was less favorable for African-Americans compared with Caucasians in these trials, other outcomes measured were considerably more similar than those seen in the population at large, suggesting that earlier detection and adjuvant therapy could appreciably improve colon cancer prognosis for African-Americans. Continued investigations into causes of the deficits noted are warranted. [J Natl Cancer Inst 1999;91:1933–40]

Colon carcinoma is the second most common cause of cancer mortality in the United States and will account for roughly 48,000 deaths in 1999, representing 10% of all cancer deaths (1). The aging U.S. population and greater frequency of disease screening will likely increase the prevalence of colon cancer in coming years.

Factors related to prognosis after colon (or colorectal) cancer include age at diagnosis, sex, site of tumor and other disease features, socioeconomic factors including treatment quality, and, most importantly, stage of disease at diagnosis (2–5). Five-year survival rates adjusted for age- and race-specific life expectancy (relative survival rates) for the years 1989 through 1994 ranged from 93.6% for localized disease to only 9.2% for colon cancer that has progressed to distant metastatic sites (6). Race has also been examined in relation to colon cancer prognosis in national health surveillance statistics and individual studies, and findings indicate that Caucasian Americans (whites) have had a more favorable survival prognosis than African-Americans (blacks) during the past several decades (6–10). For example, data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) yield 5-year relative survival rates for the period 1989–1994 for all stages of colon cancer of 64% for whites and 52% for blacks (6). The most commonly suspected explanatory factors for this difference are disparities in stage of disease at diagnosis and quality and extent of medical care between these populations.

In this study, we examined survival and related outcomes after treatment of primary colon cancer among African-American and Caucasian patients (from the United States and Canada) participating in randomized clinical trials of the National Surgical Adjuvant Breast and Bowel Project (NSABP). The randomized clinical trial design restricts the extent of disease at study entry and provides for uniform therapy, thus controlling for two major confounding factors in the relationship between race and colon cancer prognosis and allowing for other determinants of prognosis to then be investigated.

Methods

Patient Selection

The NSABP studies are a series of multicenter, randomized clinical trials with headquarters in Pittsburgh, PA, since 1971. Beginning in 1977, a series of trials evaluating adjuvant therapies for colon and rectal cancers have been conducted. In this investigation, we included data from five serially conducted studies for operable colon cancer enrolling patients from 1977 through 1994. These trials were designed hierarchically from previously obtained results and thus have specific similarities that facilitate the aggregation of data from the five trials into a larger database for this analysis. Active follow-up has been maintained for all
trials, with the exception of the first trial described below, which has terminated follow-up for patients upon their reaching at least 10 years of observation.

NSABP protocol C-01 was designed to determine if the addition of methyl-
lomustine, vincristine, and 5-fluorouracil (denoted as MOF) or immunotherapy with Bacille Calmette-Guérin (BCG) after surgery improved outcomes over those among patients treated by surgery only. From 1977 through 1983, a total of 1166 patients were accrued. Protocol C-02 compared postoperative portal venous infusion of 5-fluorouracil (5-FU) and heparin with surgery alone among 1158 patients randomly assigned from 1984 through 1988. Protocol C-03 compared adjuvant 5-FU and levamisole (5-FU + LEV) with the combination of these therapies (5-FU + LV + LEV) and with the combination of these therapies (5-FU + LV + LEV). From 1989 through 1990, a total of 2151 patients were entered. Protocol C-05 compared adjuvant 5-FU + LV with 5-FU and leucovorin (5-FU + LV) with MOF, with 1081 patients entered. Protocol C-05 compared adjuvant 5-FU + LV with 5-FU + LV and interferon alfa-2a (5-FU + LV + IFN) among 2176 patients accrued from 1991 through 1994.

Eligibility criteria for the studies were similar. In protocols C-01, C-03, C-04, and C-05, patients must have had a curative resection of adenocarcinoma of the colon and were required to have a Dukes’ stage B, i.e., T3–4, N0, M0 according to tumor–node–metastasis (TNM) classification (11), or stage C, i.e., TNM T1–4, N1–3, M0 tumor. In protocol C-02, where randomization occurred before surgery, patients were required to have a potentially curable adenocarcinoma of the colon as documented by barium enema or biopsy. A higher ineligibility rate was expected because of the discovery of benign or stage D disease at surgery (Dukes’ A patients were eligible). In all studies, patients with a contained perforation or obstruction were eligible, but patients whose tumors demonstrated free perforation were not. For entry in the study, patients must have had an Eastern Cooperative Oncology Group performance status of 2 or less and adequate renal and hepatic functions. Further details of the design of the studies, as well as primary findings, can be found in published reports (12–16).

We selected for inclusion in this analysis all protocol-eligible patients with follow-up information whose race was reported as either white (Caucasian) or black (African-American). Twenty patients with missing information in regard to number of positive lymph nodes were excluded. Eligibility violations were most often due to errors in staging prior to randomization. Proportions of protocol-ineligible patients did not differ by race. Compliance to assigned drug regimens was also similar between the groups. For protocol C-02, all patients with Dukes’ stage A disease were excluded, since the other trials consist only of patients with Dukes’ stage B or C disease. Among the five trials, data were available on a total of 5969 white and 663 black patients.

Many characteristics of the patient populations were similar across trials, with some important exceptions (Table 1). More black patients were enrolled in protocol C-01 (17.9%) than in the other trials, in which 8.2%–9.4% of enrolled patients were black. Patients in protocol C-02 had earlier stage disease (57% were Dukes’ stage B) and were considerably older than patients from the other studies. Protocol C-03 has the smallest proportion of negative-node patients

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**Table 1. Characteristics of patients in colon cancer adjuvant therapy trials**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Protocol C-01</th>
<th>Protocol C-02</th>
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<th>Protocol C-04</th>
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<td>Dukes’ C (1–4)</td>
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*See text and (11) for definition of disease staging.
†The right colon includes the cecum, ascending colon, and hepatic flexure. The left colon includes the transverse colon, splenic flexure, and descending colon.
‡BCG = bacille Calmette-Guérin; MOF = methyl-lomustine, vincristine, and 5-fluorouracil; 5-FU = 5-fluorouracil.
§See text for a definition of these categories.
(27.8% compared with 40% in the other studies). In each study, about 45% of patients were female.

**Study End Points and Statistical Methods**

Frequency distributions of selected characteristics were compared between African-Americans and Caucasians by chi-squared and Fisher’s exact tests. Two-sample t tests and Wilcoxon rank-sum tests were used to compare means or medians of continuous distributions. Time-dependent end points were as follows: 1) recurrence-free survival (RFS) time, defined as time from surgery until colon cancer recurrence, with other events treated as censored observations; 2) disease-free survival (DFS) time, defined as time from surgery until either colon cancer recurrence, (b) occurrence of a new primary cancer, or (c) death prior to recurrence or occurrence of a new primary cancer; and 3) survival time, defined as time from surgery until death from any cause. Distributions of RFS, DFS, and survival time were estimated with the use of Kaplan–Meier curves and compared by use of two-sided log rank tests over all available follow-up time (17,18). The text cites 5-year percentages from these event time distributions.

We assessed the prognostic influence of individual covariates by computing average annual rates of failure over discrete strata (e.g., age, groups). The Cox proportional hazards model was used to compute relative hazard of failure for blacks versus whites and to assess and control for the confounding influence of other prognostic covariates simultaneously (19,20). P values from these analyses are two-sided.

Analyses were first conducted within trials to estimate event time distributions and black/white relative hazards of failure for the event time end points. To compute event time distributions among patients from all trials, the method of direct adjustment was used to produce estimates, taking into account the unequal distributions of blacks and whites represented in the individual studies (21). Subsequently, data were combined, and analyses were conducted in two ways: 1) stratified Cox models, using the protocol as the stratifying factor, to control for factors intrinsic to the studies that may influence the relationship between outcome and race and to allow for a separate baseline risk of failure by study; and 2) analysis unstratified and combined into one large dataset. Results of these two analyses were compared for consistency.

For the stratified and combined analyses of patients from all protocols, treatment groups were combined as follows into three groups: group 1—surgery alone or surgery plus immunotherapy in protocols C-01 and C-02; group 2—regimens containing 5-FU as the primary active agent (MOF in protocols C-01 and C-03 and 5-FU portal vein infusion in protocol C-02); and group 3—regimens containing 5-FU plus agents (LV or LEV) that have proved additionally beneficial (5-FU + LV in protocols C-03, C-04, and C-05; 5-FU + LEV and 5-FU + LV + LEV in protocol C-04; 5-FU + LV + IFN in protocol C-05).

**RESULTS**

**Characteristics of African-Americans and Caucasians With Colon Cancer**

Table 2 shows the distribution of characteristics by race for patients combined across protocols C-01 through C-05. Whites were slightly older, with about 53% being 60 years old or older, compared with about 47% of blacks (P = .003). Whites were more often male (55.3%) than blacks (46.2%) (P<.001). Whites more often had tumors located in the rectosigmoid colon (36.7% for whites versus 26.4% for blacks), whereas blacks had more tumors in the left colon (27% for blacks versus 19.8% for whites) (P<.001). Most notably, no difference in stage of colon cancer (Dukes’ stage B versus Dukes’ stage C) or number of positive lymph nodes was apparent between African-Americans and Caucasians. When characteristics were compared by race within individual studies, similar results were seen (not shown).

**RFS, DFS, and Survival Within Individual Trials**

Initially, RFS, DFS, and survival times were compared between blacks and whites within each of the trials, irrespective of treatment group or patient characteristics. Comparisons controlling for treatment and patient characteristics are presented later.

Among patients in the first two trials (protocols C-01 and C-02), which evaluated systemic therapy relative to surgery only, 5-year RFS and DFS were similar for whites and for blacks (Table 3). Survival distributions were less similar in protocol C-02.

**Results:**

- **Characteristics of African-Americans and Caucasians With Colon Cancer**
  - Table 2 shows the distribution of characteristics by race for patients combined across protocols C-01 through C-05.
  - Whites were slightly older, with about 53% being 60 years old or older, compared with about 47% of blacks (P = .003). Whites were more often male (55.3%) than blacks (46.2%) (P<.001). Whites more often had tumors located in the rectosigmoid colon (36.7% for whites versus 26.4% for blacks), whereas blacks had more tumors in the left colon (27% for blacks versus 19.8% for whites) (P<.001). Most notably, no difference in stage of colon cancer (Dukes’ stage B versus Dukes’ stage C) or number of positive lymph nodes was apparent between African-Americans and Caucasians. When characteristics were compared by race within individual studies, similar results were seen (not shown).

- **RFS, DFS, and Survival Within Individual Trials**
  - Initially, RFS, DFS, and survival times were compared between blacks and whites within each of the trials, irrespective of treatment group or patient characteristics. Comparisons controlling for treatment and patient characteristics are presented later.

**Results:**

- **Characteristics of African-Americans and Caucasians With Colon Cancer**
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  - Whites were slightly older, with about 53% being 60 years old or older, compared with about 47% of blacks (P = .003). Whites were more often male (55.3%) than blacks (46.2%) (P<.001). Whites more often had tumors located in the rectosigmoid colon (36.7% for whites versus 26.4% for blacks), whereas blacks had more tumors in the left colon (27% for blacks versus 19.8% for whites) (P<.001). Most notably, no difference in stage of colon cancer (Dukes’ stage B versus Dukes’ stage C) or number of positive lymph nodes was apparent between African-Americans and Caucasians. When characteristics were compared by race within individual studies, similar results were seen (not shown).

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- **RFS, DFS, and Survival Within Individual Trials**
  - Initially, RFS, DFS, and survival times were compared between blacks and whites within each of the trials, irrespective of treatment group or patient characteristics. Comparisons controlling for treatment and patient characteristics are presented later.

Among patients in the first two trials (protocols C-01 and C-02), which evaluated systemic therapy relative to surgery only, 5-year RFS and DFS were similar for whites and for blacks (Table 3). Survival distributions were less similar in protocol C-02.

**Results:**

- **Characteristics of African-Americans and Caucasians With Colon Cancer**
  - Table 2 shows the distribution of characteristics by race for patients combined across protocols C-01 through C-05.
  - Whites were slightly older, with about 53% being 60 years old or older, compared with about 47% of blacks (P = .003). Whites were more often male (55.3%) than blacks (46.2%) (P<.001). Whites more often had tumors located in the rectosigmoid colon (36.7% for whites versus 26.4% for blacks), whereas blacks had more tumors in the left colon (27% for blacks versus 19.8% for whites) (P<.001). Most notably, no difference in stage of colon cancer (Dukes’ stage B versus Dukes’ stage C) or number of positive lymph nodes was apparent between African-Americans and Caucasians. When characteristics were compared by race within individual studies, similar results were seen (not shown).

- **RFS, DFS, and Survival Within Individual Trials**
  - Initially, RFS, DFS, and survival times were compared between blacks and whites within each of the trials, irrespective of treatment group or patient characteristics. Comparisons controlling for treatment and patient characteristics are presented later.
C-01, with 63% of white patients surviving to 5 years compared with 54% of black patients \((P = .11)\). For protocol C-02, which consisted of more patients with earlier stage disease, survival percentages were similar for whites and for blacks.

Among the trials evaluating different systemic chemotherapy regimens, blacks had similar to slightly less favorable RFS and DFS compared with whites (Table 3). Differences in survival were somewhat larger in patients from protocol C-04 (73% whites and 67% blacks at 5 years) and protocol C-05 (77% whites and 71% blacks).

Comparisons for Patients Combined Across Studies

For subsequent analyses, all trials were combined. First, Kaplan–Meier estimates of event time distributions were computed. Because the relative proportion of blacks and whites differs by trial and the relative prognosis of the two groups varies among the trials, we then computed weighted estimates of RFS, DFS, and survival for blacks and whites by using the proportion of the total cohort that each study constitutes as the weighting factor.

The unweighted Kaplan–Meier estimates for the combined data from protocols C-01 through C-05, ignoring treatment and other prognostic covariates, yielded the following results: Five-year RFS was 70% for whites and 67% for blacks \((P = .07)\); 5-year DFS was 62% for whites and 58% for blacks \((P = .05)\); 5-year survival was 72% for whites and 65% for blacks \((P = .001)\). The weighted estimates were more similar between blacks and whites. Five-year RFS was 70% for whites and 68% for blacks \((P = .23; \text{Fig. 1})\); 5-year DFS was 62% for whites and 60% for blacks \((P = .29)\); 5-year survival was 72% for whites and 68% for blacks \((P = .01; \text{Fig. 1})\).

Race and Other Factors in Relation to Colon Cancer Prognosis

Factors in addition to race that may be associated with RFS, DFS, or survival were investigated (Table 4). Increasing age at diagnosis was found to be associated with increasing risk of death and DFS, most likely as a result of the increased risk of new primary cancers and non-cancer deaths among older patients. The presence of and number of positive lymph nodes were strongly associated with increased risk of colon cancer recurrence and death. Males generally had worse survival and DFS but not a worse RFS. The existence of multiple sites for the primary tumor was associated with increased risk of recurrence and death, relative to tumors in the left, right, or rectosigmoid colon. Patients with tumors in the rectosigmoid colon had lower mortality rates than patients with tumors at other sites.

Fig. 2 shows black/white relative hazards for colon cancer recurrence and death, adjusted for treatment group, number of positive lymph nodes, age, sex, and location of tumor. Estimated relative hazards are shown within individual trials and from a stratified estimate for all patients, with a stratification factor defined as the trial from which the patient originated. Also shown is a similar estimate obtained from the combined data, ignoring the trial in which the patient participated. The stratified or combined analyses resulted in a relative hazard estimate generally consistent with that of the individual trials, but with increased precision. Results indicate a statistically nonsignificant 8% (95% confidence interval [CI] = −6% to 25%; \(P = .27\)) excess risk of colon cancer recurrence and a 21% (95% CI = 6%–37%; \(P = .004\)) excess risk of overall mortality for blacks (Fig. 2).

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**Tumor location**

Significantly, for mortality, patients with rectosigmoid tumors had significantly lower hazard than those with tumors in the right colon.

**Table 4. Relative hazards for disease recurrence and death in relation to additional prognostic factors for colon cancer in patients in adjuvant therapy trials**

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<thead>
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<th>Age group, y</th>
<th>No. of patients</th>
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<td>73.1</td>
<td>0.92</td>
<td>0.82–1.03</td>
<td>70.4</td>
<td>1.36</td>
<td>1.21–1.52</td>
</tr>
</tbody>
</table>

**Sex**

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Recurrence rate*</th>
<th>Relative hazard†</th>
<th>95% CI‡</th>
<th>Death rate*</th>
<th>Relative hazard†</th>
<th>95% CI‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>3026</td>
<td>74.7</td>
<td>1.00</td>
<td>Referent</td>
<td>62.5</td>
<td>1.00</td>
<td>Referent</td>
</tr>
<tr>
<td>Male</td>
<td>3606</td>
<td>77.8</td>
<td>1.06</td>
<td>0.97–1.16</td>
<td>70.7</td>
<td>1.19</td>
<td>1.09–1.29</td>
</tr>
</tbody>
</table>

**Stage (No. of positive lymph nodes)**

| Dukes’ B (none) | 2763            | 39.9             | 1.00             | Referent| 37.2        | 1.00             | Referent |
| Dukes’ C (1–4)  | 2892            | 84.3             | 2.07             | 1.86–2.31| 71.1        | 1.72             | 1.57–1.90|
| Dukes’ C (≥5)   | 977             | 200.9            | 4.71             | 4.16–5.32| 165.0       | 3.90             | 3.49–4.36|

**Tumor location**

| Right colon    | 2740            | 76.7             | 0.76             | 0.58–0.99| 74.1        | 0.81             | 0.64–1.04|
| Left colon     | 1362            | 75.9             | 0.79             | 0.61–1.04| 62.4        | 0.76             | 0.59–0.98|
| Rectosigmoid   | 2366            | 74.4             | 0.76             | 0.58–0.99| 59.9        | 0.72             | 0.56–0.92|
| Multiple locations# | 158          | 106.9            | 1.00             | —        | 93.9        | 1.00             | —        |
| Unknown        | 6               | 58.1             | —                | —        | 93.5        | —                | —        |

* Rates are (events/person years at risk) x 1000 over the first 5 years after surgery.
† Relative hazards with 95% confidence intervals are from a stratified Cox model, with protocol as the stratum, and are adjusted for treatment and the other factors in the table.
‡ CI = confidence interval.
§ See text and (11) for definition of disease staging.
¶ Includes those with unknown number of positive nodes.
The right colon includes the cecum, ascending colon, and hepatic flexure. The left colon includes the transverse colon, splenic flexure, and descending colon.
# Relative hazard comparison of multiple sites category versus other sites. Hazard of recurrence among right colon, left colon, and rectosigmoid did not differ significantly. For mortality, patients with rectosigmoid tumors had significantly lower hazard than those with tumors in the right colon.

**Treatment Effects in African-Americans and Caucasians**

Although the number of African-Americans in any one trial is small and there are interpretational difficulties associated with estimating treatment benefit across different studies, we nonetheless evaluated, both within individual trials and over the combined data, the effect of adjuvant therapy among blacks and whites and attempted to determine if these effects were similar.

In protocols C-01 and C-02, a modest survival and DFS benefit and a somewhat larger RFS benefit for adjuvant 5-FU-based therapy were seen in both blacks and whites. In protocol C-03, the 5-FU + LV arm was superior overall and among whites, although this benefit was not apparent among blacks, since black patients receiving MOF had marginally better outcomes. In protocol C-04, the 5-FU + LV arm prevailed over the 5-FU + LEV arm among both blacks and whites. In protocol C-05, no benefit for the addition of IFN to 5-FU + LV was realized for either blacks or whites.

Combining data from the trials allows for greater precision in treatment effect estimates in blacks because of the larger number of patients, but certain interpretational limitations result because of the confounding between protocol and treatment regimen, in that the regimens are not uniformly represented across the studies. Adjustment for potential confounding factors that differ across studies cannot fully alleviate this problem. Thus, we cannot assess in an unbiased manner the benefit of certain regimens, such as 5-FU + LV, compared with other regimens, such as surgery only. For protocols C-01 and C-02, both of which consisted of surgery only or surgery plus 5-FU treatment groups, data were combined and a modest benefit in the range of a 4%–14% relative reduction in colon cancer recurrence and mortality was seen for the 5-FU-containing regimens relative to treatment by surgery only. This benefit was apparent in both African-Americans and Caucasians. For the trials including regimens using 5-FU and additional agents (protocols C-03 through C-05), the outcomes appeared superior to those seen in the earlier trials, but no formal comparisons are presented.

**DISCUSSION**

Using clinical trials data to investigate differences in outcome between racial/ethnic groups offers several advantages over the use of other data sources. First, stage of disease is comparable within the constraints of the protocol entry criteria. Second, treatment and follow-up care are conducted according to a uniform standard. Finally, detailed information on prognostic covariates, such as the number of positive lymph nodes, is collected. One major drawback of data from clinical trials is the small number of participants of many racial groups, including African-Americans. Even when the proportion of black entrants to a trial matches that of the population at large, say, in the United States, an approximate 9:1 ratio of whites to blacks will be obtained. Another disadvantage is the lack of detailed socioeconomic information on patients, which may explain the outcome disparities. In the clinical trial setting, however, we anticipate that the implicit control that the trial design affords for stage and treatment would render these factors less important.

On this latter point, it is interesting to note that some studies (22, 23) have found differences in extent of treatment between black and white patients with colon cancer, often with attendant poorer outcomes for blacks; in contrast, in studies among patients with relatively uniform care (24–26), outcomes were appreciably more similar. Quality of care is associated with socioeconomic status and, thus, indirectly with race. We would expect that, with uniform care for patients with disease at a comparable location,
In this large cohort of individuals treated for colon cancer and observed during the past 15 years, African-Americans and Caucasians had largely similar demographic and clinical characteristics. Stage of disease at diagnosis was similar, owing in part to the entry criteria of the trials. The number of positive lymph nodes among lymph node-positive patients was equally similar. Other characteristics that might suggest a difference in prognosis were as follows: age, with black patients tending to be younger at diagnosis; sex, with more female patients among blacks; and location of the primary tumor, with whites more frequently having tumors in the rectosigmoid colon, a phenomenon noted by others (29,30). However, none of these factors appeared to exhibit a particularly strong influence on prognosis (Table 4).

Perhaps because of these similarities, RFS comparisons showed only a slightly less favorable prognosis for blacks, which was not statistically significant. DFS, which includes new primary cancers and deaths from non-cancer causes as events, was also lower among blacks, and there were proportionally more deaths prior to cancer recurrence comprising DFS among these patients, although the discrepancy was not large. However, overall survival differed significantly, possibly as a result of greater all-cause mortality and non-cancer mortality, as well as shorter survival time after colon cancer recurrence. The presence of concurrent adverse health conditions, or comorbidity, has been shown to increase cancer mortality (31). Excess risk of mortality was about 21% (95% CI = 6%–37%) for African-Americans, whereas excess risk of DFS or RFS was under 10%. Similar findings regarding mortality were recently reported by Dominitz et al. (25), who noted that blacks with colorectal cancer had a 13% higher risk of mortality over their white counterparts in an equal-access health care system setting.

Because we did observe overall mortality differences between blacks and whites in this trial, while colon cancer recurrence was largely similar, we speculated that mortality due to other chronic diseases might be more frequent among blacks. Detailed, reliable information on cause of death was not ascertained for this analysis, and studies have indicated problems with using reported cause-of-death information without careful review (32,33). As mentioned above, when events comprising DFS were compared, blacks were somewhat more likely to have died prior to colon cancer recurrence or to the occurrence of a new primary cancer. Thus, although we do not currently present a detailed analysis of mortality by cause, it is plausible that mortality rates for chronic diseases other than cancer may contribute to the shorter overall survival times among blacks.

The benefit of adjuvant chemotherapy, where noted, appeared to extend to black patients as well as to white patients, although the ability to detect heterogeneous response to therapy is limited because of the small number of black patients in any one study, while assessment of regimens for the combined data is difficult to interpret because differences cannot be attributed solely to treatment. While African-American and Caucasian patients from the recent trials have improved 5-year relapse-free probability and survival compared with those from the earlier trials, after differences in stage at diagnosis and other prognostic variables are taken into account, factors in addition to treatment also differ across studies. For example, after the first trial (C-01), the number of hospitals contributing patients was greatly expanded and began to include more institutions serving communities with higher incomes. Outside the clinical trial setting, differences between blacks and whites in extent of care for other cancers and
chronic diseases have been widely noted (34–36). However, it is sometimes not possible to fully assess in these retrospective studies why specific therapies may have been forgone for certain cancer patients. For instance, it may have been that procedures were omitted as a result of an already advanced stage of disease at diagnosis. Uniformity of care stemming from a common clinical stage and specific prospective treatment plan may be a contributing factor to the similarities in outcome seen in the NSABP studies.

More advanced stage of disease at diagnosis remains the most glaring deficit for African-Americans with colon cancer in the population at large, since, like most cancers, this disease presents a rapidly deteriorating prognosis with more advanced stage, regardless of care. The well-documented excess of more advanced cancers among African-Americans has been attributed to socioeconomic disparities (which affect the poor of any racial/ethnic group) and could likely be reduced by increased and targeted screening (37–39). Diversity in clinical research participation has been enhanced through NCI programs beginning in the late 1980s. Enrollment in NCI-sponsored trials was examined in the 1990s and was found to be proportionally representative of the population at large (40). Nonetheless, recent efforts have been appropriately directed toward strategies for increased enrollment of African-Americans into randomized clinical trials (41,42). This goal should be recognized as serving a dual purpose: 1) It is a mechanism by which quality care in accordance with current treatment guidelines [see, for example, (43)] and access to potentially beneficial new agents can be enjoyed by a traditionally under-served population, and 2) this increased diversity in enrollment will provide the information necessary to identify causes of variation in prognosis and response to therapies according to race or other demographic factors, guiding future research and care delivery.

REFERENCES

(22) Ball JK, Elixhauser A. Treatment differences between blacks and whites with colorectal cancer. Med Care 1996;34:970–84.


NOTES

1Editor’s note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a bimonthly basis, and the NCI makes the data available to the public for scientific research.

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