Differences in Breast Cancer Prognosis Among African-American and Caucasian Women

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Abstract
This review explores factors potentially contributing to the disparity in survival after breast cancer between African-American and Caucasian women in the United States. A number of factors have been implicated as the cause of poorer survival for black women, including clinical and pathologic features of the disease that are indicative of poor prognosis, economic resource inequities, and differences in treatment access and efficacy. The latter is explored in detail using data from the National Surgical Adjuvant Breast and Bowel Project (NSABP), a nationwide multicenter clinical trials group for breast and colorectal cancers.

Key studies into the disparity in breast cancer survival are reviewed according to proposed principal determinants of poorer outcome for black women. Results among black and white women participating in several randomized NSABP clinical trials are also presented. Primary endpoints in those studies were clinical and pathologic disease characteristics at study entry, time to disease progression or new cancers, and total survival time after breast cancer diagnosis and treatment.

In most studies reported in the literature, the primary explanatory factor alone, such as stage of disease at diagnosis, did not fully account for differences in outcome between groups; when additional factors were taken into account, however, prognoses became more similar. Results from the NSABP clinical trials similarly indicated that when stage of disease and treatment were comparable, outcomes for blacks did not differ markedly from those of whites.

In summary, black women, diagnosed at comparable disease stage as white women and treated appropriately, tend to experience similar breast cancer prognoses and survival. However, important clinical and pathologic disease characteristics may continue to place certain women at increased risk of poorer outcome, and warrant continued study. The opportunity for increased clinical trial participation by black women is encouraged. (CA Cancer J Clin 2000;50:50-64.)

Introduction
Breast cancer is the most common malignancy among females in the United States. This year, approximately 184,200 new cases of female breast cancer will be diagnosed, and more than 40,000 deaths will be attributed to the disease. Although white women have a higher incidence of breast cancer than blacks, mortality rates for black women meet or exceed those of whites, indicating a poorer survival experience for black women. Results from several large-scale cancer surveillance studies conducted over the past few decades have confirmed this survival disadvantage.

Data from the End Results Program of the National Cancer Institute found five-year breast cancer survival rates adjusted for race and age-specific all-cause mortality (called relative survival rates)
of 47% for blacks and 64% for whites for the period between 1960 and 1967, and 51% for blacks and 65% for whites between 1968 and 1973. Data from the Surveillance, Epidemiology, and End Results (SEER) program showed improvement for both groups between 1973 and 1979, yet the survival deficit for blacks remained.

Figure 1 shows yearly age-adjusted breast cancer incidence and mortality rates for the period from 1973 to 1996, reported by the SEER program. Rising incidence in both groups and the greater incidence in whites over the period can be seen, as well as equal or greater mortality for blacks from 1980 to 1994. The approximately 3% increase in breast cancer mortality among all patients between 1980 and 1990 is in part due to an 18% increase in mortality among blacks. Beginning in 1990, a trend towards declining mortality overall and for white women is seen, as has been recently reported. It should be noted, however, that mortality for black women has thus far largely remained constant, with a small decline in mortality appearing after 1995.

This report presents historic and recent research concerning breast cancer prognosis among black and white women, highlighting results from a large body of articles investigating the complex web of clinical, pathologic, social, economic, and demographic factors that may contribute to poorer outcomes for African-American women. Areas with potential for intervention, such as early detection and adequate characterization of disease stage and pathology, will be emphasized, and the
role of clinical trials in improving treatment for black women will be explained.

Research efforts towards understanding this problem will be described using data from the National Surgical Adjuvant Breast and Bowel Project (NS-ABP), a large multicenter clinical trials group that evaluates surgical, radiation, chemotherapy, and endocrine treatments for breast and colorectal cancers.

Factors Implicated in Poorer Breast Cancer Prognosis Among Black Women

Factors potentially related to differential breast cancer prognosis for black and white women are many and varied, and include clinical characteristics, biologic aspects of the disease, socioeconomic status, and related health care factors. Historic and recent literature regarding the influence of these factors on breast cancer survival for black and white women are classified here into broad categories, although most studies necessarily explore several factors concurrently.

Stage of Disease at Diagnosis

The stage of the primary breast cancer at diagnosis remains the foremost determinant of ultimate outcome. Indeed, the benefit obtained from effective treatments is modest compared with the predictive effect that disease stage has on prognosis. Patients with metastatic breast cancer have a relatively poor prognosis, and even effective therapies may add only months of life. In contrast, breast cancer that is confined to the breast and axillary lymph nodes (node-positive breast cancer) is treatable in many cases, although long-term prognosis for these patients is still markedly poorer than for women whose disease is completely confined to the breast without evidence of lymph node involvement (node-negative disease).

Data from many national surveys and health statistics sources have indicated that black patients are more frequently diagnosed with a more advanced stage of breast cancer than are white patients. Figure 2, which is based on 1996 SEER program data, shows stage of disease at diagnosis and indicates a greater proportion of higher-stage cases among black women. Numerous retrospective and prospective epidemiologic studies have confirmed this observation.

The obvious question, therefore, is to what degree does difference in stage at diagnosis alone account for poorer outcomes for black women? Secondary questions relate to whether more advanced stage at diagnosis is wholly due to lack of access to or utilization of health care resources—which would result in later detection of disease—or is due, in part, to more aggressive forms of the disease being more common among black women.

Regardless of the reasons black women are more frequently diagnosed with later-stage disease, many investigators have sought to determine whether outcomes are similar among black and white patients of comparable stage. In most studies where black and white patients with the same stage of breast cancer are compared, however, some residual disparity in outcome remains and, for a given stage, black women more often exhibit disease characteristics associated with poorer prognosis.

In one of the largest studies that examined stage of disease at diagnosis, Natarajan and colleagues used a portion of data from the 1982 American College of Surgeons National Survey to analyze breast cancer survival by race. Data reported on 2,296 black and 24,265 white patients from 565 hospitals in a long-term survey, and on 1,571 black and 17,701 white patients in a short-term survey were included. Information was obtained on demographic characteristics, disease stage and pathology, treatment, and specific patient history, such as method of tumor discovery, menopausal status, use of...
Larger tumor size, greater nodal involvement, and estrogen receptor (ER)-negative tumors occurred with greater frequency in black women. Outcomes for patients stratified by nodal status showed significantly increased survival rates for whites. Race remained a prognostic factor after taking into account stage, age, and tumor characteristics, suggesting that black/white survival differences are only partially explained by differences in stage and related factors.

A similar retrospective analysis of 2,322 white and 536 black patients, sampled from female residents in metropolitan Atlanta with a diagnosis of breast cancer between 1978 and 1982, found that blacks were younger at diagnosis, had larger tumors, more nodal involvement, and more advanced-stage disease. Among similarly treated patients with advanced disease, survival rates for blacks were lower than for whites. Among women with node-negative disease, blacks still had slightly lower survival rates.

More recent studies in women with early-stage disease have also demonstrated that blacks with stage I disease had shorter times to recurrence and lower overall survival rates than whites. Results from the National Cancer Institute’s Black/White Cancer Survival Study (BWCSS) indicated that among breast cancer patients from three US metropolitan areas, stage at diagnosis only partially accounted for differences in survival. A recent study using SEER data tracked breast cancer stage at diagnosis through the 1980s, finding a shift toward earlier stage at diagnosis, probably due to screening efforts. Nevertheless, this trend differed by race, with black women remaining less likely to be diagnosed at an early stage. A subsequent study examining survival patterns showed that black women who were diagnosed at younger ages bore a higher probability of dying of breast cancer within five years of the diagnosis. Since competing causes of death are more prevalent at older ages, breast cancer takes its greatest toll—in terms of
years of life lost—on younger women. Several studies have demonstrated that black women tend to be younger at diagnosis, and this study further illustrates poorer outcomes for these women relative to whites of the same age.\textsuperscript{13}

Like age, obesity has been identified as both a risk factor for breast cancer and a contributing factor to poorer prognosis.\textsuperscript{14,15} In a recent study, obesity was found to be more prevalent among black women with breast cancer, and was associated with more advanced disease stage in both blacks and whites.\textsuperscript{16} These findings were conjectured to be due to the effect of obesity on endogenous hormone levels, which can also affect progression of the disease.\textsuperscript{17} Other potential contributing factors have been suggested, such as greater difficulties in clinical detection of breast disease in obese patients.

These and many other studies have shown that African-American women are more frequently diagnosed with breast cancer at a more advanced stage, and that this stage difference is a major factor in poorer prognosis for these women. It is also clear from most studies, however, that some disparity exists after accounting for stage differences, and that additional factors also contribute to outcome differences.

**Disease Characteristics in Addition to Stage**

In addition to disease stage, there are specific pathologic breast tumor characteristics that may account for black/white differences in outcomes.

**Hormone Receptors and Cell Differentiation**

Among characteristics that differ in favor of whites are the presence of hormone receptors on tumor cells and degree of cell differentiation. Estrogen receptors and progesterone receptors, for example, are important both as independent indicators of prognosis—with ER-negative tumors exhibiting more aggressive growth—and as a basis for selecting treatment. Specifically, patients whose tumors are characterized as ER-positive are candidates for the antiestrogen tamoxifen (or similar agents), while patients with ER-negative tumors are often given chemotherapy.

Numerous studies have found differences in tumor ER- and progesterone-receptor (PR) content between black and white patients, with black patients less frequently having ER- and PR-positive tumors.\textsuperscript{6,10,17-20} A survey by the American College of Surgeons found that 71% of whites had ER-positive tumors compared with only 58% of blacks.\textsuperscript{6} In a study of estrogen receptors, progesterone receptors, and pathologic features from tissue samples of 146 black female breast cancer patients from Howard University Hospital, poorly differentiated and ER-negative tumors were found more frequently than in the white population at large.\textsuperscript{18}

A comparison of estrogen and progesterone receptors among patients in Birmingham’s University Hospital found that blacks were significantly more likely to have ER- and PR-negative tumors.\textsuperscript{19} Likewise, an analysis of participants in the NCI’s BWCSS found blacks significantly more likely to have tumor characteristics associated with poor prognosis, such as lack of hormone receptors, high-grade nuclear atypia, and poorly differentiated tumors, compared with whites with the same disease stage.\textsuperscript{20}

A survey of tumor specimens submitted to the University of Texas again found that ER- and PR-negative tumors with higher S-phase fraction were more common in black patients.\textsuperscript{17} And, one study has suggested that ER negativity is associated with a particularly high risk for black patients, while for whites with ER-negative tumors and for all patients with ER-positive tumors, outcomes were significantly more favorable.\textsuperscript{10}

Results from these studies offer compelling evidence that other disease characteristics contribute to poorer prognosis for black women, even when stage
of disease is comparable. However, comparability of stage and standard of treatment must be established before these more subtle effects can be adequately evaluated.

**TYPE AND QUALITY OF SCREENING/TREATMENT**

Appropriate treatment for operable breast cancer, according to current recommendations of consensus panels periodically convened by the National Institutes of Health or of independent experts in the field, include surgery, with radiation therapy after breast-conserving procedures, generally followed by some type of systemic treatment, either hormonal therapy, chemotherapy, or a combination.\(^{21,22}\) In the 1980s, the recommendation for adjuvant therapy was first made for node-positive patients only, and later was extended to node-negative patients with specific disease features. For example, by the late 1980s, node-negative patients with ER-negative tumors were found to benefit from chemotherapy while ER-positive patients were found to benefit from tamoxifen.

Two dimensions of the contribution of treatment to differences in prognosis can be examined. First, some studies have investigated whether suitable care was provided uniformly to black and white patients, including adequate diagnostic procedures and therapy recommendations in accordance with national guidelines. Second, the question of whether efficacy of established therapies differs by racial groups has been addressed, in an attempt to identify so-called treatment by race interaction.

With respect to treatment quality for breast cancer patients, McWhorter and Mayer\(^{23}\) investigated the relationship between race, treatment received, and survival using 36,905 cases from nine registries of the SEER program. Blacks were significantly less likely to have received surgical treatment, which may have been partially due to the greater prevalence of cases with inoperable, advanced disease. However, differences in treatment persisted after adjustment for age, stage, and histology, possibly accounting for the survival disadvantage in blacks noted in the SEER survey.

In a study evaluating quality of care for breast cancer patients among hospitals in Illinois, late-stage diagnosis was more frequent in urban hospitals and among patients with poor insurance coverage.\(^{24}\) More interesting was the observation that omission of important diagnostic tests and radiation therapy was more frequent in urban hospitals, suggesting a greater degree of nonstandard care in the urban facilities examined. A prospective evaluation of treatment plans for stage II breast cancer patients participating in the NCI's BWCSS found similar treatment recommendations for blacks and whites, which were generally in accordance with national guidelines.\(^{25}\) However, a subsequent analysis of this same cohort revealed that certain aspects of care differed according to factors such as age and race, with older and black patients less frequently receiving treatment in accordance with recommended guidelines.\(^{26}\)

**Similar Care, Similar Outcomes**

Studies in which comparable treatments were administered, such as in clinical trials or single institution studies, tend to show similar outcomes between blacks and whites. A recent study that followed 1,037 white and 481 African-American women who were uniformly treated reported very similar outcomes, but continued to note that black women more frequently had larger tumors and positive nodes, resulting in a small survival disadvantage.\(^{27}\) Another study of black women treated for breast cancer at the Cook County Hospital in Chicago found that node-negative patients treated surgically had recurrence and mortality rates comparable to those published for white patients treated elsewhere.\(^{28}\) In that study, black patients with
node-positive tumors who were treated with chemotherapy and/or tamoxifen achieved a degree of benefit similar to that seen for white patients. A more recent study of blacks and whites receiving comparable screening, treatment, and follow-up care through a large metropolitan health maintenance organization showed similar breast cancer survival rates. Likewise, a large multicenter clinical trial evaluating chemotherapy for patients with node-positive breast cancer found a similar benefit among black and white patients. Outcomes for black and white patients in NSABP clinical trials will be discussed later in this report.

Access to Breast Cancer Screening
Some studies have specifically addressed the potential of improving access to breast cancer screening to reduce disparity in outcomes. In a Health Insurance Plan of New York study, participants were randomized to either a screening group where periodic examinations were provided, or to a control group where patients received their usual care with no particular emphasis on breast cancer screening. Five-year relative survival rates indicated that mortality due to breast cancer was lower in the screening group by nearly 40%, with white and black patients having roughly equal survival rates. In the control group, however, mortality rates differed substantially by race.

In 1988, early results of a breast cancer screening program instituted in an urban Chicago hospital showed a significant increase in the percentage of women receiving mammograms, compared with the period prior to screening, when only 2% of the eligible population received mammograms. Comparing early and late periods of the breast screening implementation, a significant trend toward greater detection of localized disease was seen. However, several issues remain to be resolved concerning effective screening in this population, as recent studies have found differences in mammographic screening rates that do not satisfactorily explain later-stage diagnosis among African Americans. Similarly, delay in treatment-seeking or delay in care caused by greater time from consultation to diagnosis and treatment recommendation were not shown to be major contributing factors in stage differences between blacks and whites. Regardless of the role of screening in the past, as well as in time to detection, recent evidence shows significantly increased mammography use rates in black women.

Social and Economic Factors
In addition to treatment access, other economic and social factors related to health status and health care utilization represent possible explanations for the disparity in outcomes. A retrospective study of breast cancer patients treated at the Harlem Hospital in New York City described a distinctly disadvantaged population compared with US blacks nationwide and particularly compared with white patients.

This dimension of the problem is most difficult to study, particularly in a retrospective manner or from large databases, which record limited information beyond disease status and ultimate outcome. Economic factors are often inferred from more general information, such as census tract data. Detailed information about the health knowledge, behaviors, and access to health care of individuals is not measured directly. Few studies have directly ascertained factors related to poverty, education, delay in seeking and accessing care, and fewer still have addressed factors related to social support and coping.

Two early studies that implicated socioeconomic status as a confounding factor in poor survival for black women—one conducted among 4,618 white and 912 black patients treated at the MD Anderson Cancer Center in Houston between 1949 and 1968, and the other from the
Medical College of Virginia among 515 white and 388 black breast cancer patients treated between 1968 and 1977—found a strong association between race, low economic status, and poor survival.41,42

Data from the Western Washington Cancer Surveillance System in Northwest Washington state were used to study the effect of social class and race on breast cancer survival among patients diagnosed between 1973 and 1983.43 Measures of socioeconomic status, such as the percentage of individuals below the poverty level, percentage of high school graduates, percentage of female-headed households, and other indicators were developed for each patient’s residence based on 1980 census block group information. Results showed that race was not a predictor of survival after age, stage, and social class indicator differences were taken into account.

In a similar study using 1990 census tract information to establish socioeconomic measures for 1,132 white and 253 black patients with primary breast cancer diagnosed between 1974 and 1985, socioeconomic status alone was highly predictive of survival and disease-free survival, while race was not predictive after adjustment for socioeconomic status and other factors.44

A 1986 study examined the relationships among income, stage at diagnosis, and race in breast cancer cases reported to the New York State Cancer Registry between 1976 and 1981.45 A comparison of disease stage among 4,443 black and 47,198 white patients indicated that blacks were more likely to present with regional or metastatic disease at time of diagnosis. Black/white differences in disease stage by per capita income of the resident county showed a significant association, with the disparity in stage being minimal among women from higher income areas. A related study in 1990 that studied breast cancer in higher income black women confirmed this association.46 Black women from this higher income community were only about 1.15 times as likely as US whites to die from breast cancer. Adjustment for age and other characteristics would be expected to further reduce this rate.

Similar findings were obtained when data from the SEER program were examined according to race and income status.47 A strong association between disease stage at diagnosis and income level was noted, with black and white women of the same income category having essentially similar stage distributions. A similar study conducted among cases from the Connecticut Tumor Registry showed an association between socioeconomic status—defined as percent high school graduates present in the relevant census tract—and stage at diagnosis, and confirmed the finding that among women of higher socioeconomic status, stage of disease at diagnosis was similar between blacks and whites.48

As might be expected, most indices of poverty are associated jointly with poor prognosis and more advanced stage of disease at diagnosis, making it difficult to parse out separate effects. These studies have drawn the anticipated conclusion that poverty adversely affects cancer prognosis independently of racial status, and that economic and resource equity would greatly contribute to an improved outcome for black women with breast cancer. As Harold Freeman, MD, Chairman of the President’s Cancer Panel, has noted, race is largely a social rather than biologic construct in the US, and can serve as a weak discriminant of outcome at best once its confounders are accounted for.49,50

Findings from NSABP Clinical Trials

NSABP studies, a series of multicenter randomized clinical trials administered by the University of Pittsburgh since 1971, have evaluated many aspects of breast cancer treatment, including surgical pro-
cedures, radiation therapy, chemotherapy, and endocrine therapy. Findings from these studies have profoundly affected breast cancer care, including the pioneering use of breast-conserving surgery and radiation (instead of mastectomy) and the administration of adjuvant therapy across a spectrum of node-positive and node-negative breast cancer patients both nationally and globally.

Using clinical trial data to assess differences in outcome among black and white patients affords several advantages over other data sources. First, patients are homogeneous with respect to disease stage at diagnosis, as defined in the protocol entry criteria. Second, treatment is delivered in a uniform, quality-controlled manner. Third, patients generally have minimal concurrent serious morbidity at study entry. Finally, information about relevant features, such as estrogen content and size of the primary tumor, allows consideration of important factors that contribute to prognosis. Such studies also provide the opportunity to assess treatment efficacy among black patients directly, albeit with a smaller than desirable sample, and to compare the magnitude of any benefit with that seen among white patients. On the other hand, the use of clinical trial data also involves some disadvantages, including a lack of detailed social and economic data and the small numbers of African-American participants in many of the studies, as well as the inherent danger in retrospectively examining trial results in patient subsets, which may lead to spurious findings.51

**PROGNOSIS AMONG BLACK AND WHITE WOMEN IN NSABP SURGICAL TRIALS**

**Protocol B-04: Radical versus Total Mastectomy**

In the early 1970s, the NSABP conducted a trial (Protocol B-04) to evaluate different surgical procedures for patients with breast cancer that may or may not have spread to the axillary lymph nodes. The primary goal of the study was to determine whether there was any additional benefit associated with radical mastectomy compared with total mastectomy, which is a less extensive surgical procedure. The study also evaluated the role of radiation therapy for node-negative patients who were treated with total rather than radical mastectomy. Results of this study over the last 20 years continue to indicate no difference in outcome between the less extensive and more extensive surgical procedures, and have shown that radiation is effective in preventing local tumor recurrence.

Results of this trial were analyzed for differences in outcomes between the 191 black and 442 white participants who had undergone radical mastectomy. This group was chosen because information about nodal status, which was determined pathologically, was available for these patients. Black patients were younger at diagnosis, had larger tumors, and were more likely to have positive nodes. Moreover, pathologic features of tumors associated with poor prognosis were found more frequently in black patients. For node-positive patients, outcomes for black women were worse, with 45% surviving through five years, compared with 61% of whites. Poorer prognostic factors for black patients accounted partially for this difference, and the survival rate for blacks adjusted for prognostic factor differences was within 10% of that for whites. Survival among node-negative patients was similar for the two groups, with about 85% of both black and white patients surviving for five years.

**Protocol B-06: Lumpectomy + Radiation versus Total Mastectomy**

In contrast, a subsequent NSABP study evaluating lumpectomy plus radiation compared with total mastectomy (Protocol B-06) indicated a significantly poorer prognosis among node-negative black women (74%) compared with white women (89%) at five years.9 Additional analyses indicated that tumors in black
patients were more likely to exhibit poor nuclear grade and other pathologic characteristics associated with less favorable prognosis, and were less likely to be ER- and PR-positive. The somewhat contradictory findings in these two surgical trials motivated a more detailed analysis of data from two recent trials for node-negative breast cancer patients.

**PROGNOSIS AMONG NODE-NEGATIVE BREAST CANCER PATIENTS RECEIVING ADJUVANT THERAPY**

Until the late 1980s, patients with breast cancer that was completely confined to the breast, with no evidence of spread to the lymph nodes, were considered to have sufficiently good prognoses as to preclude the need for further therapy after surgery. Results of clinical trials at the end of that decade, however, indicated that these patients could benefit from additional systemic therapy.

**Protocols B-13 and B-14: Surgery Alone versus Surgery + Chemotherapy Or Tamoxifen**

In 1982, two such trials were initiated by the NSABP. Protocol B-13, a trial for patients with ER-negative tumors [<10 femtomoles(fmol)/mg cytosol protein], compared surgical treatment alone with surgery plus 12 courses of sequential methotrexate and fluorouracil (5-FU) (M→F). Protocol B-14 compared surgery plus placebo with surgery plus long-term (five years) tamoxifen among patients with ER-positive tumors (≥10 fmol).

In 1996, results from these studies were analyzed to determine (1) whether there were differences in prognoses between black and white patients, after controlling for hormone-receptor status, treatment, and other pathologic and clinical factors; and (2) whether blacks and whites similarly benefited from the systemic therapies administered.52 Endpoints for evaluation were overall survival (time to death from any cause) or disease-free survival (time to breast cancer recurrence at any anatomic site; a new primary cancer; or death from some other cause). Results from a total of 916 white and 108 black patients from Protocol B-13, and 3,709 white and 203 black patients from Protocol B-14 were analyzed.

Examining patient characteristics at diagnosis, we found that among ER-negative patients, black women more often had PR-negative tumors. Among ER-positive patients, blacks were younger at diagnosis and had larger tumors. In both trials, blacks were more likely to have been treated with total mastectomy than with lumpectomy and radiation.

When we looked at disease-free survival in ER-negative patients, 71% of blacks remained event-free through five years, compared with 74% of white patients. Among ER-positive patients, disease-free survival for blacks was comparable to that for whites, with 81% of black patients and 80% of white patients remaining event-free at five years.

Survival for these patients was also similar. Among ER-negative patients, 83% of blacks survived through five years, compared with 85% of whites. Among ER-positive patients, 93% of blacks and 92% of whites were alive at five years. Estimated risk of breast cancer recurrence or death, taking into account differences in tumor characteristics, was also very similar.

Disease-free survival and survival by treatment group were estimated separately for blacks and whites (Fig. 3). Among patients with ER-negative tumors, five-year disease-free survival was 60% for black patients treated with surgery alone and 80% for those receiving M→F. Among white patients, five-year disease-free survival was 68% in the surgery-alone group and 76% for M→F patients.

Among patients with ER-positive tumors, five-year disease-free survival was 79% for blacks receiving placebo and 82% for blacks receiving tamoxifen. Among whites, 72% of placebo patients and 83% of tamoxifen patients were event-free at
five years. Results of survival analyses by race and treatment group similarly showed an equal degree of treatment benefit for black and white patients.

RESULTS FROM ADJUVANT THERAPY TRIALS INVOLVING NODE-POSITIVE PATIENTS

Protocol B-09: Chemotherapy plus Tamoxifen

In 1987, we used data from an NSABP study (Protocol B-09) comparing the chemotherapy drugs melphalan (L-PAM) plus 5-FU (PF) with L-PAM plus 5-FU and tamoxifen (PFT) to examine survival outcomes for blacks and whites.53 One thousand four-twentty (896 white, 146 black) stage II breast cancer patients accrued between 1977 and 1980 were included. In the PF arm, unadjusted five-year survival rates were 52% for blacks and 68% for whites, while in the PFT arm, 57% of blacks and 65% of whites were alive at five years. Tumors tended to be larger among black patients, and ER-negative tumors were found in 63% of black patients compared with 47% of white patients. Adjusted five-year survival rates for blacks (57% for PF and 61% for PFT) were not significantly different from those of whites, but still reflected slightly poorer survival after controlling for possible confounding factors.

An examination of other chemotherapy trials for node-positive patients also indicated a modest survival disadvantage for black patients, partially explained by baseline characteristics associated with poorer prognosis. Where benefit was noted for a given treatment regimen, black and white patients appeared to benefit equally over their counterparts receiving the comparison regimen.

Discussion

Several studies have shown that when breast cancer stage of disease and treatment are comparable, outcomes for African-American and white patients are largely similar.27-30 Likewise, when disease stage and socioeconomic status, which is correlated with quality of care, are comparable, outcomes for black patients are greatly improved and resemble those of whites.43,44,46 Residual differences noted in many studies may be due to other factors, such as heterogeneity in disease features—which impart greater risk for blacks, even after controlling for disease stage and treatment. Other, as yet unidentified factors, may also contribute to poorer outcomes for some patients. Increasingly, however, evidence from genetic epidemiology does not support the notion that there would be sufficient racial homogeneity to expect profoundly distinct disease characteristics or treatment response strictly on the basis of race.54

Results from our detailed study of node-negative breast cancer indicated that times to disease recurrence and survival among blacks and whites in our clinical trials are similar.52 Comparisons of treatment efficacy among blacks and whites separately indicated that a similar benefit was achieved, particularly for ER-negative patients. These results—combined with findings from other studies that support the benefit of early breast cancer detection and show that black and white patients confined to a similar stage and similarly treated have similar outcomes—suggest that early detection, followed by appropriate therapy, could appreciably reduce the disparity in outcome. On the other hand, comparisons of patient characteristics at diagnosis examined in all of our studies confirm other findings that African-American women more frequently have characteristics associated with poorer prognosis. Additionally, we noted small racial disparities in outcome throughout the trials involving node-positive patients.

In the population at large, treatment quality remains an important concern with regard to breast cancer prognosis for all women. Currently, treatment choice is
Patients with ER-negative tumors received either no further treatment or 12 courses of sequential methotrexate/fluorouracil. Patients with ER-positive tumors received either placebo or tamoxifen. Curves represent the percentage of patients alive and free of breast cancer recurrence or new cancers over the time period represented by the horizontal axis.
made in accordance with known indicators that place patients at particular risk, and so it is vital that adequate clinical and pathologic characterization of the disease be performed at diagnosis. It may be that more African-American women than white women of a given disease stage will be found to be eligible for adjuvant chemotherapy, given our (as well as those of others) observations that black women often have indicators of poor prognosis at diagnosis. To reduce or eliminate differences in outcomes among these patients, it is imperative that established therapies be uniformly delivered to all women in accordance with their anticipated clinical prognoses.

We observed in our trials that, where either procedure was acceptable, black women were much more likely to have received total mastectomy rather than lumpectomy with radiation therapy. This finding may have many explanations, including lack of adequate radiation therapy programs at institutions where black patients are treated; lack of resources, time, and/or access to enable selection of radiation therapy as an option; preference on the part of black patients; surgeon’s preference; and numerous other factors. One study showed frequency of breast-conserving surgery to be related to higher income and education, but not independently to race. While breast-conserving surgery has been shown to be equivalent to more extensive procedures for managing breast cancer, the lesser frequency of its use may be an indirect measure of other health care indicators related to outcome, and requires further investigation.

At the time that the NSABP studies described in this report were accruing, no special efforts were made to enhance participation of black patients. A tacit assumption when examining black/white differences in these studies is that the randomized clinical trial setting provides a degree of control for factors related to quality of care, since treatment and follow-up care are carefully monitored.

In recent years, the NSABP and other clinical trial groups have undertaken programs to increase participation of traditionally under-represented patients in randomized clinical trials. Despite concerns about minority participation, a study of racial/ethnic representation in NCI-funded clinical trials found participation of blacks and Hispanics commensurate with their respective percentages in the general population. Nonetheless, changes mandated by Congress through the NIH Revitalization Act of 1993 have brought about increased minority recruitment efforts at the NCI. Such participation in randomized clinical trials may represent a way to offer better quality care, while at the same time ensuring that study results can more appropriately be generalized to the population of all women.

All federally funded clinical trials meet ethical standards that require that new agents having potential benefit be compared against current standard therapy, so that participants are assured of receiving the best proven therapy at a minimum, and may have the opportunity to receive agents that are not available outside the clinical trial setting. Quality assurance of treatment delivery is incorporated into the study design and monitoring of such trials. A greater representation of African-American women in clinical trials could serve both individual patients and the scientific community in its efforts to answer the important public health question of why some women have poorer outcomes.

Despite these recommendations, there are often significant barriers to entry among these women, including the failure of physicians to offer clinical trial participation and reticence on the part of some patients, which is understandable given some of the unfortunate historical events involving African-Americans and medical research in the US.

Focused efforts by African-American scientists and community leaders will
increase awareness and lead to new approaches for improving this situation.\textsuperscript{60} In addition to recruitment of minorities by clinical trial groups and other researchers, investigators should continue to study—where feasible using existing databases—the potential for increased risk of recurrence and death among black women with breast cancer.

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