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CLINICAL INVESTIGATION **Breast**

OUTCOMES IN BLACK PATIENTS WITH EARLY BREAST CANCER TREATED WITH BREAST CONSERVATION THERAPY

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Background: The race-specific impact of prognostic variables for early breast cancer is unknown for black patients undergoing breast conservation.

Methods and Materials: This was a retrospective study of 1,231 consecutive patients ≥40 years of age with Stage I–II invasive breast cancer treated with lumpectomy and radiation therapy at the University of Chicago Hospitals and affiliates between 1986 and 2004. Patients were classified as either black or nonblack. Cox proportional hazards regression was used to model the effects of known prognostic factors and interactions with race.

Results: Median follow-up for surviving patients was 82 months. Thirty-four percent of patients were black, and 66% were nonblack (Caucasian, Hispanic, and Asian). Black patients had a poorer 10-year overall survival (64.6% vs. 80.8%; adjusted hazard ratio [HR], 1.59; 95% confidence interval [CI], 1.23–2.06) and 10-year disease-free survival (58.1% vs. 75.4%; HR 1.49; 95% CI, 1.18–1.89) compared with nonblack patients. Tumor sizes were similar between nonblack and black patients with mammographically detected tumors (1.29 cm vs. 1.20 cm, $p = 0.20$, respectively). Tumor size was significantly associated with overall survival (HR 1.48; 95% CI, 1.12–1.96) in black patients with mammographically detected tumors but not in nonblack patients (HR 1.09; 95% CI, 0.78–1.53), suggesting that survival in black patients depends more strongly on tumor size in this subgroup. Tests for race-size method of detection interactions were statistically significant for overall survival ($p = 0.049$), locoregional control ($p = 0.036$), and distant control ($p = 0.032$) and borderline significant for disease-free survival ($p = 0.067$).

Conclusion: Despite detection at comparable sizes, the prognostic effect of tumor size in patients with mammographically detected tumors is greater for black than in nonblack patients. © 2011 Elsevier Inc.

Breast neoplasm, Continental population groups, Mammography, Outcome assessment, Health care.

INTRODUCTION

Breast cancer mortality has been declining for all women since 1990, but the magnitude of this decrease has been greater for white than for black patients (1). Racial disparity in breast cancer outcomes is a well-recognized problem (2–5). A variety of factors, including poorer socioeconomic status (SES) (5–7), higher incidence of competing comorbid diseases (8, 9), biologic differences in tumor characteristics (10–14), lower use of screening mammograms (15–18), and inequality of treatment (3, 19–21), have been proffered to explain the poorer outcomes observed in black patients. However, even when controlling for these and other known prognostic factors, black patients continue to have worse breast cancer–specific mortality (3, 7, 8).

The decline in breast cancer mortality has been attributed in part to both screening mammography (15, 22–27) and improvements in adjuvant therapy (15). However, the magnitude of the decrease in breast cancer mortality differs by race, with Caucasian women experiencing a 2.4% yearly decline since 1990, compared with only 1.1% in African-American women since 1991 (1). The reason for this discrepancy is unclear. Although historically, black women have been less likely than Caucasian women to use screening mammograms (15), in recent years such use by black women has reached the same level as that by Caucasian women (1), indicating that mammography underuse is unlikely to explain racial disparities in current trends.

Black patients with breast cancer are more likely to be classified as having lower SES, but defining SES is notoriously difficult, and no consensus on the most suitable definition has been reached (5–7). Low SES has been associated with lower use of screening mammography (17, 10) and poor outcomes (28, 29). However, a recent meta-analysis examining

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race and SES concluded that, even when controlling for age, stage, and SES, race is an independent indicator of breast cancer mortality (7).

A higher prevalence of comorbid disease in black patients has also been posited to explain disparities in outcomes. A recent study of patients with Stage I–IV breast cancer reported that black patients were more likely than white patients to have adverse comorbid diseases, which explained differences in all-cause and competing-cause mortality (8). However, race was still independently associated with both recurrence and breast cancer mortality when controlling for the effects of comorbid disease.

An equally complicated question has been the role of biology with regard to racial differences in the natural history of breast cancer (30–32). Tumors in African-American women are more likely to be estrogen receptor (ER)/progesterone receptor (PR) negative and to have high grade, a high mitotic index, alterations of p53, and the basal-like phenotype (5, 10–13, 32–35). Whether these differences are due to an inherently more aggressive tumor phenotype or simply to later presentation of disease, or both, is unclear.

Recently, an analysis of three of the largest randomized controlled trials for screening mammography in North America revealed that interval cancers are associated with poor outcomes (36). Whether interval cancers occur more commonly in black patients is not known, but adverse pathologic features, such as a higher growth fraction, alteration of p53, and lower apoptotic fraction, are correlated with later presentation of disease (37) and are more common in interval clinically detected cancers appearing in mammographically screened populations (33, 38, 39). Thus, investigating potential differences in biologic tumor characteristics by race and method of detection is an increasingly important area of research.

Comprehensive analyses of factors contributing to racial disparities in outcome in early breast cancer are limited. We sought to examine a racially diverse cohort of patients undergoing breast conservation with lumpectomy and radiotherapy, with or without adjuvant systemic therapy, whereby differences due to advanced presentation of disease, access to treatment, and variability of therapy were minimized. Particular attention was given to interactions between race and known prognostic factors. In so doing, preliminary analyses indicated a differential benefit from screening mammography among women who had already been screened, and further analysis focused on the nature of this discrepancy.

METHODS AND MATERIALS

Patient eligibility

The study sample consisted of 1,231 consecutive patients treated at the University of Chicago and affiliated hospitals between January 1986 and May 2004. All patients had American Joint Committee on Cancer clinical or pathologic Stage I–II breast cancer and were treated with breast conservation surgery followed by whole breast irradiation, with or without systemic therapy. This database concerned recurrence and cosmesis in women undergoing breast conservation; data for women who underwent mastectomy were not available. We excluded women with ductal carcinoma *in situ* without evidence of microinvasion, noncarcinoma histology, or bilateral breast cancer and patients with a history of other cancer within the previous 10 years, other than nonmelanomatous skin cancer.

Surgical therapy

Surgery consisted of partial mastectomy. Axillary staging was either an axillary lymph node (LN) dissection or a sentinel LN procedure followed by axillary dissection as appropriate. In most cases when margins were found to be positive, the patient underwent reexcision. Margins were defined as positive if the tumor extended to the inked margin.

Radiation therapy

Patients were treated with whole breast radiation therapy (RT) with a boost to the tumor bed. All fields were treated daily, 5 days a week. Patients were treated in the supine position with tangential fields with additional supraclavicular field at the discretion of the treating physician.

Systemic therapy

Systemic chemotherapy consisted of various regimens including cyclophosphamide, methotrexate, fluorouracil, anthracyclines, and taxanes, at the treating physician's discretion. Typically, patients received adriamycin and cyclophosphamide, with or without a taxane (AC $\pm$ T), CAF (cyclophosphamide, adriamycin, and fluorouracil), or CMF (cyclophosphamide, methotrexate, and fluorouracil).

Patients with either estrogen receptor or progesterone receptor positive by immunohistochemistry were scored as hormone receptor positive. Adjuvant therapy with tamoxifen was recorded, but the use of aromatase inhibitors was not standard for most of the study period, and data on their use were not available.

Follow-up evaluation

After the completion of therapy, patients were seen in clinic at 3- to 6-month intervals for the first 2 years and at 6-month intervals for the first 5 years. Thereafter, patients were seen yearly. Unilateral mammograms were obtained every 6 months on the affected breast, and bilateral mammograms were obtained yearly. Chest radiographs and liver function tests were obtained yearly in the absence of symptoms or findings worrisome for metastatic spread, and more extensive testing was undertaken as appropriate to the clinical situation.

Definitions

Race was self-described by the patient at the time of initial consultation. Tumors were recorded as ''mammographically detected'' if they were detected by screening mammogram and were not associated with clinical signs. Patients were stratified into ''low'' or ''high'' SES by estimating the median household income for each patient, using census tract data. Patients below the median household income for the group were recorded as being of ''low'' SES. Comorbid disease was self-reported by the patient and was scored in a binary fashion based on whether the patient had hypertension, diabetes mellitus, coronary artery disease, or chronic obstructive pulmonary disease.

Statistical analysis and definition of endpoints

Comparisons of demographic and tumor characteristics between groups were performed using the chi-square test or Fisher's exact test (if the number of patients in a given cell was <5) for proportions, and the unpaired *t*-test or analysis of variance (for >2 groups) for