

RACIAL AND ETHNIC DISPARITIES IN BREAST CANCER STAGE, TREATMENT, AND SURVIVAL IN THE UNITED STATES

Christopher I. Li, MD, PhD

Several studies indicate that African-American, Hispanic White, and Native American women with breast cancer present with more advanced stages and have poorer survival rates than non-Hispanic Whites, while Asians/Pacific Islanders do not. However, Asians/Pacific Islanders and Hispanic Whites are heterogeneous populations, and recent data indicate that certain subgroups of these populations have poorer breast cancer outcomes compared to non-Hispanic Whites, while others have better outcomes. Many of these disparities have persisted for decades, but until recently, detailed studies exploring the reasons behind these disparities have been limited. The results of these studies point to the effect of differences in socioeconomic status, access to health care (including both breast cancer screening and treatment services), lifestyle factors, and tumor characteristics on these disparities. Thus, these studies indicate that these disparities are multifactorial, and therefore strategies aimed at reducing them must involve advocacy, research, education, and healthcare services. A key component to the success of these strategies is not only support for them on the federal and state levels, but also the involvement of local communities in developing programs and policies that are culturally and linguistically appropriate for their communities in order to ensure not only the utility, but also the longevity, of these efforts. (*Ethn Dis.* 2005; 15[suppl 2]:S2-5-S2-9)

Key Words: Breast Carcinoma, Ethnicity, Race, Stage, Survival, Treatment

From the Fred Hutchinson Cancer Research Center, Division of Public Health Sciences, Seattle, Washington.

Address correspondence and reprint requests to Christopher Li, MD, PhD; Fred Hutchinson Cancer Research Center; Division of Public Health Sciences; 1100 Fairview Avenue North, M4-C308; P.O. Box 19024; Seattle, WA 98109-1024; 206-667-4630; 206-667-5938 (fax); cili@fhcrc.org

BACKGROUND

Breast cancer remains the most commonly diagnosed cancer among women in the United States and worldwide. An estimated 215,990 cases of breast cancer will be diagnosed in the United States in 2004, representing 32% of all cancers in women.¹ However, breast cancer incidence rates vary widely by race/ethnicity. From 1996–2000, White women had a breast cancer incidence rate of 140.8/100,000.² However, rates were 14% lower (121.7/100,000) among African Americans, 31% lower (97.2/100,000) among Asians/Pacific Islanders, 36% lower (89.8/100,000) among Hispanics/Latinos, and 59% lower (58.0/100,000) among American Indians/Alaska Natives. Breast cancer mortality rates also vary by race/ethnicity. For example, though African Americans have a lower incidence of breast cancer compared to Whites, their breast cancer mortality rate is 32% higher than that of Whites (35.9/100,000 vs 27.2/100,000).

RACIAL/ETHNIC DISPARITIES IN BREAST CANCER STAGE AND SURVIVAL

Several studies have evaluated disparities in breast cancer stage and survival by race/ethnicity. With respect to stage, data from 1996–2000 indicate that the proportions of all breast cancer cases diagnosed at a regional or distant stage were higher among African Americans (45% of all cases), Hispanics/Latinos (42%), and American Indians/

Alaskan Natives (44%) compared to Whites (34%).² Alternatively, Asians/Pacific Islanders had a similar proportion of regional/distant stage breast cancer (35%) compared to Whites. With respect to survival, African-American women have experienced lower 5-year breast cancer survival rates compared to White women for the past several decades. Among Whites, 5-year survival rates have improved from 75% in 1974–1976, to 79% in 1983–1985, and finally to 88% in 1992–1999. Among African Americans, 5-year survival rates also improved from 63% in 1974–1976, to 64% in 1983–1985, and finally to 74% in 1992–1999. While the improvements in 5-year survival rates among African Americans are encouraging, the survival rate for African-American women in 1992–1999 was still lower than it was for White women in 1974–1976. Hispanic Whites^{3–8} and Native Americans^{6,9} also have poorer breast cancer survival rates compared to non-Hispanic Whites. However, in the aggregate Asians/Pacific Islanders have been observed not to differ with respect to breast cancer survival compared to non-Hispanic Whites.^{3,4}

Several studies suggest that breast cancer stage and survival may vary across the different groups of women included in the heterogeneous category of Asians/Pacific Islanders. Studies conducted in San Francisco³ and Hawaii^{10,11} indicate that Hawaiian and Filipino women are more likely to be diagnosed with advanced-stage breast cancer and to have poorer survival rates after diagnosis compared to non-Hispanic Whites. Two of these studies also found that Japanese and Chinese women pre-

sent with less advanced stages of breast cancer and have better survival rates compared to non-Hispanic Whites. These studies were limited by relatively small sample sizes, their ability to evaluate other Asian/Pacific Islander subgroups, and their generalizability, since they only included women from two different areas of the United States.

DIFFERENCES IN BREAST CANCER STAGE, TREATMENT, AND SURVIVAL, 1992–1998

Background and Methods

In order to provide a recent update of the relationship between race/ethnicity and three breast cancer outcomes, stage, treatment, and survival, and to evaluate differences across various Asian/Pacific Islander and Hispanic White subgroups that had not been previously studied, we recently published the results of a retrospective cohort study based on data from the 11 population-based tumor registries that participate in the Surveillance, Epidemiology, and End Results (SEER) Program.¹² Our cohort included 123,934 women 20 years of age and older diagnosed with a first primary invasive breast cancer between January 1992 and December 1998. The cancer registries included were those serving the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the urban areas surrounding Atlanta, Georgia; Detroit, Michigan; Los Angeles, California; San Francisco-Oakland, California; San Jose-Monterey, California; and Seattle, Washington. All data used in this study, including race and ethnicity data, were solely based on the information abstracted from patient medical records by SEER. Further operational details and methods used by the SEER program are provided elsewhere.¹³

Our primary variable of interest was race/ethnicity. Beginning in 1988, in addition to categorizing race/ethnicity as

White, Black, American Indian/Alaskan Native, Chinese, Japanese, Filipino, and Hawaiian, SEER added categories for Korean, Vietnamese, and Asian Indian/Pakistani among others. In 1988 SEER also added information about Spanish surname or origin, specifically coding whether individuals were Mexican, Puerto Rican, Cuban, South or Central American (except Brazil), other specified Spanish/Hispanic origin (includes European), or Spanish/Hispanic (no origin specified). The SEER program also provides information on tumor characteristics (including American Joint Committee on Cancer [AJCC] stage) and surgical and radiation treatments (though not on adjuvant chemotherapy or hormonal therapy). While information on marital status is provided, data on other sociodemographic factors, such as income and health insurance status, are not.

In addition to evaluating stage and mortality, we were also interested in assessing whether or not the primary surgical and radiation treatments given to women of different races/ethnicities with stage I and II breast carcinomas <5.0 cm met the standards of care outlined by the 2000 NCCN practice guidelines¹⁴ and the 1990 National Institutes of Health Consensus Development Conference,¹⁵ by using methods consistent with previous reports.^{16,17} We classified women as having received standard primary treatment if they received: 1) breast conserving surgery (BCS) with axillary lymph node dissection and radiotherapy; or 2) a total mastectomy (including simple, modified radical, radical, and extended radical mastectomies) with axillary lymph node dissection. Women were classified as receiving inappropriate primary treatment not meeting the standard of care if they had: 1) a subcutaneous mastectomy; 2) BCS without radiation; 3) BCS without axillary lymph node dissection; or 4) a total mastectomy without axillary node dissection.¹⁶

Results and Interpretation

We observed that African-American, Native-American, and Hispanic White women had elevated risks of advanced-stage (70%–150% increases) breast cancer and death (10%–70% increases) compared to non-Hispanic Whites. However, we found substantial variations within the groups of women categorized as Asians/Pacific Islanders and Hispanic Whites. Among Asians/Pacific Islanders, Japanese women had reduced risks of stage III and IV breast cancers, while Hawaiian, Vietnamese, and Indian/Pakistani women had elevated risks compared to non-Hispanic Whites. Also, Japanese and Chinese women had reduced risks of death while Hawaiian and Vietnamese women had elevated risks. Among Hispanic Whites, Mexicans, South/Central Americans, and Puerto Ricans each had elevated risks of stage IV breast cancer, but the magnitudes of these risks varied from a 60% increase among South/Central Americans to a 260% increase among Puerto Ricans. All three Hispanic White groups also experienced elevated risks of death.

Few studies have evaluated risks of receiving inappropriate treatment by race/ethnicity. Among women with stage I and II breast cancer, we found that African Americans, Mexicans, and Puerto Ricans were 20%–50% more likely to receive inappropriate treatment compared to non-Hispanic Whites. Alternatively, Japanese, Chinese, Korean, and Vietnamese women were all 20%–40% less likely to receive inappropriate treatment compared to non-Hispanic Whites.

Though our study was limited because race/ethnicity data were based on medical record reviews, and we lacked data on important potential confounders such as socioeconomic status and access to health care, we confirmed the findings of previous studies and demonstrated that disparities in stage and survival by race/ethnicity have persisted through 1998 in the United States. Our findings also expanded on previous

work because we were able to evaluate risks among women of different racial/ethnic sub-groups in a large, multi-site, population-based setting. Here we provide some of the first evidence that Indians/Pakistanis, Mexicans, South/Central Americans, and Puerto Ricans are more likely to present with advanced-stage breast cancer. Additionally, with regard to survival, we document that Hawaiians, Mexicans, South/Central Americans, and Puerto Ricans have greater risks of death compared to non-Hispanic Whites.

Another strength of this study is that we were able to evaluate how primary treatments administered to breast cancer patients differ by race/ethnicity. Though most women receive care meeting current standards, and the proportion of women with breast cancer undergoing breast conservation is increasing, the proportion of women receiving inappropriate care is rising in the United States.¹⁶ Our results demonstrate that, while certain racial/ethnic groups were less likely to receive the standard of care, including Blacks, Mexicans, and Puerto Ricans, certain Asian/Pacific Islander subgroups were more likely to receive such care.

WHY DO THESE DISPARITIES EXIST?

Disparities in breast cancer outcomes, including stage, treatment, and survival, by race/ethnicity, persist in the United States. Several possible hypotheses for these disparities have been explored in numerous investigations.

Differences in socioeconomic status (SES) have been suggested as one of the primary explanations for disparities in breast cancer stage and survival by race/ethnicity. Studies exploring this factor have focused primarily on differences between African Americans and Whites, and in general, they have consistently found that adjustment for SES attenuates Black/White stage and survival dif-

ferences. One study observed that the 3.0-fold (95% confidence interval [CI]: 1.9- to 4.7-fold) elevation in risk of late-stage breast cancer that African Americans experienced compared to the risk seen in White women was attenuated to a 1.8-fold (95% CI: 1.1-fold to 3.2-fold) elevation in risk when adjusted for SES.¹⁸ Another found that the 100% and 50% elevations in risk of distant-stage breast cancer that Blacks and Hispanics, respectively, experienced compared to the risk seen in Whites were attenuated to 50% and 10% elevations in risk, respectively, when adjusted for sociodemographic factors.¹⁹ Similar results have been observed with respect to survival; one study observed that the elevated risk of death in Blacks was attenuated from a relative risk (RR) of 1.26 (95% CI: 1.02–1.57) to a RR of 1.17 (95% CI: 0.95–1.38).²⁰ However, SES alone does not entirely explain the disparities that exist; even after adjusting for these factors, elevations in risk of advanced-stage cancer and death persist. In general, this finding has consistently been observed across studies. For example, a recent study of 12,063 breast cancer cases diagnosed in Detroit, Michigan, observed that African-American women had an increased risk of advanced-stage cancer even after adjusting for SES (odds ratio [OR] = 1.30; 95% CI: 1.17–1.46).²¹ Another large study from Florida also observed that both African Americans and Hispanics had elevated risks of advanced-stage breast cancer compared to non-Hispanic Whites (OR = 1.65, 95% CI: 1.39–1.97 and OR = 1.26, 95% CI: 1.07–1.49, respectively) after adjusting for both income and insurance status.²² Finally, a meta-analysis of 14 studies observed that even after adjusting for SES, African Americans had a 22% higher risk of death (95% CI: 13%–30%) compared to Whites. Thus, though SES may somewhat attenuate the elevated risks of advanced-stage breast cancer and death that women of certain races/ethnicities experience, SES alone does not

account for the entirety of these disparities.

Difference in access to health care, including both cancer screening and treatment services, is another proposed explanation for these disparities. Differences in mammography utilization rates by race/ethnicity clearly exist; 72.1% of Whites >40 years of age, but only 68.2% of African Americans, 62.6% of Hispanics/Latinos, 57.0% of Asian Americans, and 52.0% of American Indians/Alaska Natives, had a mammogram within the past two years.¹ One study estimated that 12%–30% of the excess late-stage breast cancers diagnosed among Black women is due to differences in mammography utilization rates.²³ Differences in the receipt of timely and adequate breast cancer treatment by race/ethnicity could also affect mortality disparities. One study observed that 22.4% of African-American patients experienced delays (>3 months) in breast cancer diagnosis and treatment, compared to only 14.3% of White women, even after adjusting for differences in access to care and SES.²⁴ Similar findings have been observed in other studies,^{25,26} but others found different results.^{27,28} Like our study, another recent SEER based study observed that among early-stage breast cancer patients treated with BCS, African-American women were less likely to receive follow-up radiation therapy, which is considered the standard of care for these patients.²⁹ African-American women with breast cancer also receive lower chemotherapy dose proportions (actual: expected doses) and relative dose intensities compared to those received by Whites in a multivariate adjusted analysis.³⁰ A recent review of data on racial/ethnic disparities in treatment for all types of cancer concluded that disparities exist in the receipt of definitive primary therapy, conservative therapy, and adjuvant therapy by race, and that these differences result in more frequent recurrences, shorter disease-free survival times, and higher mortality among racial/ethnic minorities.³¹

RACIAL/ETHNIC BREAST CANCER DISPARITIES - Li

Differences in the distributions of factors related to stage of breast cancer diagnosis by race/ethnicity may also, in part, account for these disparities. Of particular interest has been the role of obesity, since proportions of women who are obese vary widely by race/ethnicity. One study observed that obesity was associated with an elevated risk of advanced-stage breast cancer (OR = 3.10, 95% CI: 1.28–7.52); this study found that adjusting for obesity reduced the risk of late-stage breast cancer that Blacks had compared to Whites from an OR of 1.98 (95% CI: 1.22–3.19) to an OR of 1.66 (95% CI: 1.01–2.73).³²

Finally, biologic differences in the breast tumors diagnosed among Whites vs Blacks have been suggested as an explanation for the survival differences between the two groups. For example, one study observed that, stage for stage, African-American breast cancer patients have higher proportions of grade III tumors and lower proportions of grade I and II tumors.³³ A review of studies evaluating differences in breast cancer tumor characteristics among African Americans and Whites found that, in addition to being higher grade and more poorly differentiated, tumors diagnosed among African Americans were also more likely to be estrogen-receptor negative, to have more aggressive histologies, and to have higher S-phase fractions, all of which are associated with poorer outcomes.³⁴ A recently published study of Atlanta women also found that African-American women are more likely to be diagnosed with breast carcinomas that overexpress cyclin E, p16, and p53, and to have low expression of cyclin D1.³⁵ Thus, since the tumors that African Americans are diagnosed with tend to be more aggressive, this finding could partially account for their survival disadvantage.

SUMMARY AND CONCLUSIONS

Disparities in breast cancer outcomes by race/ethnicity continue to per-

sist in the United States. Each of the factors described above is likely to account for some proportion of these disparities, which points to the multifactorial nature of this public health problem. Highlighting this fact is a recent study that evaluated various factors thought to be related to these disparities, including differences in access to health care, mammography utilization, and body mass index.³⁶ It found that no single factor could explain more than half of the race-stage differences observed between Black and White breast cancer patients. Thus, multi-tiered efforts involving advocacy, research, education, and healthcare delivery that target each of the factors underlying these disparities are needed if true progress is to be made.

The differences in access to breast cancer screening and adequate treatment by race/ethnicity are solely the result of socioeconomic and cultural factors. Understanding these differences is of public health importance, since increasing the availability of screening programs targeting women of certain racial/ethnic groups, and improving the treatment regimens that those who develop cancer receive, may be valuable means of improving early breast cancer detection rates and improving survival in these populations. In principle, equal application of existing knowledge about cancer prevention, early detection, and treatment to all segments of the population should substantially reduce cancer disparities. A key component is the involvement of local communities in developing programs and policies that are culturally and linguistically appropriate to ensure not only the utility, but also the longevity, of these efforts.

REFERENCES

1. American Cancer Society. *Cancer Facts and Figures 2004*. Atlanta, Ga: American Cancer Society, Inc; 2004.
2. Ries LAG, Eisner MP, Kosary CL, et al, eds. *SEER Cancer Statistics Review, 1975–2000*. Bethesda, Md: National Cancer Institute; 2003.
3. Hsu JL, Glaser SL, West DW. Racial/ethnic

differences in breast cancer survival among San Francisco Bay Area women. *J Natl Cancer Inst*. 1997;89:1311–1312.

4. Boyer-Chammard A, Taylor TH, Anton-Culver H. Survival differences in breast cancer among racial/ethnic groups: a population-based study. *Cancer Detect Prev*. 1999;23:463–473.
5. Elledge RM, Clark GM, Chamness GC, Osborne CK. Tumor biologic factors and breast cancer prognosis among White, Hispanic, and Black women in the United States. *J Natl Cancer Inst*. 1994;86:705–712.
6. Frost F, Tollestrup K, Hunt WC, Gilliland F, Key CR, Urbina CE. Breast cancer survival among New Mexico Hispanic, American Indian, and non-Hispanic White women (1973–1992). *Cancer Epidemiol Biomarkers Prev*. 1996;4:861–866.
7. Zaloznik AJ. Breast cancer stage at diagnosis: Caucasians versus Hispanics. *Breast Cancer Res Treat*. 1997;42:121–124.
8. Bentley JR, Delfino RJ, Taylor TH, Howe S, Anton-Culver H. Differences in breast cancer stage at diagnosis between non-Hispanic White and Hispanic populations, San Diego County 1988–1993. *Breast Cancer Res Treat*. 1998;50:1–9.
9. Sugarman JR, Dennis LK, White E. Cancer survival among American Indians in western Washington state (United States). *Cancer Causes Control*. 1994;5:440–448.
10. Meng L, Maskarinec G, Wilkens L. Ethnic differences and factors related to breast cancer survival in Hawaii. *Int J Epidemiol*. 1997;26:1151–1158.
11. Meng L, Maskarinec G, Lee J. Ethnicity and conditional breast cancer survival in Hawaii. *J Clin Epidemiol*. 1997;50:1289–1296.
12. Li CI, Malone KE, Daling JR. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med*. 2003;163:49–56.
13. Young JL Jr, Percy C, Asire AJ, eds. Surveillance, Epidemiology, and End Results: Incidence and Mortality, 1973–77. *Natl Cancer Inst Monogr*. 1981;57:1–1082.
14. Carlson RW, Anderson BO, Bensinger W, et al. NCCN practice guidelines for breast cancer. *Oncology*. 2000;14:33–49.
15. Treatment of early-stage breast cancer: consensus statement. *NIH Consensus Development Conference, June 18–21, 1990*. Bethesda, Md: National Institutes of Health; 1990:8(6).
16. Nattinger AB, Hoffmann RG, Kneusel RT, Schapira MM. Relation between appropriateness of primary therapy for early-stage breast carcinoma and increased use of breast-conserving surgery. *Lancet*. 2000;356:1148–1153.
17. Ballard-Barbash R, Potosky AL, Harlan LC, Nayfield SG, Kessler LG. Factors associated with surgical radiation therapy for early stage breast cancer in older women. *J Natl Cancer Inst*. 1996;88:716–726.

18. Lannin DR, Matthews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. *JAMA*. 1998;279:1801-1807.
19. Miller BA, Hankey BF, Thomas TL. Impact of sociodemographic factors, hormone receptor status, and tumor grade on ethnic differences in tumor stage and size for breast cancer in US women. *Am J Epidemiol*. 2002;155:534-545.
20. Ansell D, Whitman S, Lipton R, Cooper R. Race, income, and survival from breast cancer at two public hospitals. *Cancer*. 1993;72:2974-2978.
21. Schwartz KL, Crossley-May H, Vigneau FD, Brown K, Banerjee M. Race, socioeconomic status, and stage at diagnosis for five common malignancies. *Cancer Causes Control*. 2003;14:761-766.
22. Roetzheim RG, Pal N, Tennant C, et al. Effects of health insurance and race on early detection of cancer. *J Natl Cancer Inst*. 1999;91:1409-1415.
23. McCarthy EP, Burns RB, Coughlin SS, et al. Mammography use helps to explain differences in breast cancer stage at diagnosis between older Black and White women. *Ann Intern Med*. 1998;128:729-736.
24. Gwyn K, Bondy ML, Cohen DS, et al. Racial differences in diagnosis, treatment, and clinical delays in a population-based study of patients with newly diagnosed breast carcinoma. *Cancer*. 2001;100:1595-1604.
25. Vernon SW, Tilley BC, Neale AV, Steinfeldt L. Ethnicity, survival, and delay in seeking treatment for symptoms of breast cancer. *Cancer*. 1985;55:1563-1571.
26. Dennis CR, Gardner B, Lim B. Analysis of survival and recurrence vs patient and doctor delay in treatment of breast cancer. *Cancer*. 1975;35:714-720.
27. Gregorio DI, Cummings M, Michalek A. Delay, stage of disease, and survival among White and Black women with breast cancer. *Am J Public Health*. 1983;73:590-593.
28. Caplan LS, Helzlsouer KJ, Shapiro S, et al. System delay in breast cancer in Whites and Blacks. *Am J Epidemiol*. 1995;142:804-812.
29. Joslyn SA. Racial differences in treatment and survival from early-stage breast carcinoma. *Cancer*. 2002;95:1759-1766.
30. Griggs JJ, Sorbero MES, Stark AT, Heining SE, Dick AW. Racial disparity in the dose and dose intensity of breast cancer adjuvant chemotherapy. *Breast Cancer Res Treat*. 2003;81:21-31.
31. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *J Natl Cancer Inst*. 2002;94:334-357.
32. Jones BA, Kasi SV, Curnen MG, Owens PH, Dubrow R. Severe obesity as an explanatory factor for the Black/White difference in stage at diagnosis of breast cancer. *Am J Epidemiol*. 1997;146:394-404.
33. Henson DE, Chu KC, Levine PH. Histologic grade, stage, and survival in breast carcinoma: comparison of African-American and Caucasian women. *Cancer*. 2003;98:908-917.
34. Trock BJ. Breast cancer in African-American women: epidemiology and tumor biology. *Breast Cancer Res Treat*. 1996;40:11-24.
35. Porter PL, Lund MJ, Lin MG, et al. Racial difference in the expression of cell cycle-regulatory proteins in breast carcinoma: study of young African-American and White women in Atlanta, Georgia. *Cancer*. 2004;100:2533-2542.
36. Hunter CP, Redmond CK, Chen VW, et al. Breast cancer: factors associated with stage at diagnosis in Black and White women. *J Natl Cancer Inst*. 1993;85:1129-1137.