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Race, Ethnicity, and the Diagnosis of Breast Cancer

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Breast cancer is not one disease, and eliminating the disparities in outcomes requires improved understanding of biology and implementation of systemwide clinical innovation to deliver high-quality care to all women, one woman at a time. Representing 14.0% of all new cancer diagnoses, an estimated 232 670 new cases of breast cancer will occur in 2014, and an estimated 40 000 women will die of the disease.[1,2] Despite significant gains in the treatment of the disease, leading to an overall reduction in breast cancer mortality, black women continue to die disproportionately from aggressive forms of breast cancer. There has been no fundamental shift in the approach to treatment for early-stage breast cancer based on biology.

In this issue of *JAMA*, Iqbal and colleagues[3] found significant differences in the likelihood of diagnosis with stage I breast cancer and risk of death among 8 ethnic/racial groups in the United States using the Surveillance, Epidemiology, and End Results (SEER) 18 registries database. Based on their analysis of 373 563 women with invasive breast cancer, including 268 675 non-Hispanic white, 34 928 Hispanic white, 38 751 black, 25 211 Asian, and 5998 other ethnicities, the authors found that black women were less likely to be diagnosed with stage I breast cancer (non-Hispanic white women, 50.8%; black women, 37.0%) and were twice as likely to die of breast cancer with small-sized tumors than non-Hispanic white women (7-year actuarial risk for death from stage I breast cancer of 6.2% vs 3.0% for white women). Asian women had the highest likelihood of being diagnosed with stage I breast cancer and a lower risk of dying compared with white women (0.8% vs 1.5%, respectively; hazard ratio, 0.60 [95% CI, 0.49-0.73]; $P < .001$). The difference between black women and non-Hispanic white women remained after adjusting for income and estrogen receptor (ER) status and was statistically significant after excluding patients with triple-negative breast cancer (ie, breast cancer cells testing negative for ER, progesterone receptor [PR], and ERBB2).

Triple-negative breast cancer is associated with a poor prognosis, especially among black women.[4] These cancers are more likely to be diagnosed at an early age (and therefore not detected by screening if current population guidelines to initiate screening at age 50 years are followed), to have metastasized to lymph nodes even when tumors are less than 2 cm in

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size, and to rapidly acquire resistance to chemotherapy, leading to shortened overall survival. As Iqbal et al[3] rightly concluded, the racial/ethnic disparities in breast cancer outcomes can in part be accounted for by differences in the biological aggressiveness of triple-negative breast cancer in black women compared with other racial/ethnic groups.

With more granular data collection by SEER that includes race/ethnicity as well as ER, PR, and ERBB2 status, ethnic minorities in the United States can no longer be grouped together. The biological differences in breast cancer by race/ethnicity, and failures in the US health care delivery system that lead to suboptimal care for black women and women of other races/ethnicities, can now begin to be addressed. Based on the findings of Iqbal et al,[3] biology alone cannot be the contributing factor creating the survival gap in breast cancer. Instead, this report should be viewed in the context of known tumor differences between black and white women, and this knowledge should be integrated into innovative quality improvement efforts in breast cancer management across the continuum of care.

With appropriate high-quality multimodality treatment (including chemotherapy and radiation therapy), aggressive breast tumors including triple-negative breast cancer are highly curable. Several studies have revealed regional variations in breast cancer mortality by race demonstrating that biology is not the only factor creating the survival disparity. Analyzing mortality data from the National Center for Health Statistics from 1975 to 2004, DeSantis et al[5] found that breast cancer death rates for white women decreased in all 50 states; however, among black women, breast cancer death rates increased in 2 states, were unchanged in 24 states, and decreased in only 11 states. States with the worst mortality rates for black women such as Tennessee, Louisiana, Illinois, Oklahoma, Washington, DC, Michigan, Mississippi, and Texas have nearly 1½ the mortality rates of Delaware (2007-2011 age-adjusted death rate of 24.2 vs 34.7 for Tennessee), where systemwide interventions to improve cancer outcomes have been implemented.[6,7]

Iqbal et al[3] found differences across all age groups in stage at diagnosis and argue that this stage disparity was more likely attributed to biology than screening factors. Even though biological factors without doubt play a role in this divergence in stage at diagnosis, there remain variations by race and ethnicity in the quality of breast cancer screening that contribute to this disparity. A study of mammography capacity and quality in a large urban setting found that the facilities that served predominantly minority women were less likely to be academic (27% vs 71%) or private (29% vs 43%) institutions, less likely to have digital mammography (18% vs 71%), and less likely to have dedicated breast imaging specialists reading the films (23% vs 87%).[8] Each of these characteristics is associated with higher-quality care for women with breast cancer.

Iqbal et al[3] also found that the probability of death among women with breast cancer with small-sized tumors was significantly higher for black women compared with white women. It must be argued, therefore, that beyond the biology, patterns-of-care factors also contribute to poorer outcomes for black women. Delays in treatment,[9] misuse of treatment through non–guideline-concordant therapy,[10,11] and underuse of treatment[12,13] have all been demonstrated to affect the care of black women with breast cancer. For example, Bickell et al[14] conducted a study that explored racial disparity in the underuse of adjuvant breast

cancer treatment, including omission of radiotherapy after breast-conserving surgery, omission of adjuvant chemotherapy after resection of hormone receptor–negative tumors of 1 cm or larger, and omission of hormonal therapy for hormone receptor–positive tumors of 1 cm or larger, and found racial disparities in all 3 adjuvant therapies assessed. These quality failures in treatment delivery occur for therapies that have been demonstrated to improve disease-free and overall survival in large randomized trials.

Beyond screening and treatment differences, failures in the delivery and development of novel interventions must be addressed. The study by Iqbal et al[3] demonstrates likely intrinsic differences in the aggressiveness of the tumors between black and white patients. Hall et al[15] reported that among 46 276 participants (3.8% with African ancestry and 78.3% with Western European ancestry), *BRCA1* and *BRCA2* mutation prevalence was 10.2% and 5.7% in the African ancestry group, respectively, vs 6.9% and 5.2% in the Western European ancestry group. A recent study that assessed targeted genomic capture and next-generation sequencing found that 65 of 289 (22%; 95% CI, 18%-28%) black women with breast cancer referred to a cancer risk clinic had inherited at least 1 damaging mutation in known breast cancer susceptibility genes that increased their risk for breast cancer.[16] Thus, there is evidence of a high rate of inherited mutations in genes that might explain increased risk for young-onset aggressive breast cancers in black women.

However, this fertile research area, which could potentially lead to a personalized approach to risk assessment, prevention, and early detection, is limited by gaps in referrals of minority patients to cancer risk clinics. Armstrong et al[17] found that white women with a family history of breast and ovarian cancer were 5 times more likely to undergo genetic evaluation than black women with a similar history. In addition, minority women have had limited access to clinical trials, and some trials have collected inadequate sociodemographic and comorbidity information that could be integrated with tumor biology and genomics data to better examine predictors of racial/ethnic differences in outcomes.[18]

There is an unprecedented opportunity to deliver high-quality precision medicine regardless of race/ethnicity or socioeconomic status. Access to the use of genetic or molecular markers to guide choice of targeted therapy and reduce the costs of care can be made more equitable. For women with triple-negative disease, access to prompt diagnosis and initiation of chemotherapy can be lifesaving because these tumors metastasize early. Closing the survival gap will only occur once health care leaders initiate system changes that improve access to high-quality care along with a more comprehensive study of breast cancer biology through inclusion of a substantial number of minority patients in “omics” research and in clinical trials.

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