Clinical Cancer Research

CCR Translations
Commentary on O'Brien et al., p. 6100

Toward a Better Understanding of Race and Cancer

Otis W. Brawley

A better understanding of breast cancer subtypes is allowing their use as prognostic markers. For some time, it has been documented that black women with breast cancer have a poorer prognosis than white women of the same stage. Advances in immunohistochemistry and the appreciation of breast cancer subtypes are enabling investigators to study the distribution of these subtypes among populations. *Clin Cancer Res; 16(24); 5920–2. ©2010 AACR.*

In this issue of *Clinical Cancer Research*, O'Brien and colleagues (1) use the North Carolina Breast Cancer Study to assess distributions of breast cancer subtypes among black and white women. This is an extremely valuable cohort study having a median follow-up of 9 years. The authors use relatively simple immunohistochemical staining to categorize tumors into subtypes. They correlate these subtypes with outcomes and demonstrate that tumor subtype is a legitimate prognostic marker. Unlike previous studies, this one assesses not only estrogen receptor, progesterone receptor, and HER2 status but also HER1 and CK5/6 status. This allows for classification of tumors as

- luminal A (ER+ and/or PR+,HER2−),
- luminal B (ER+ and/or PR+, HER2+),
- HER2+, ER−, PR−,
- basal-like (ER−, PR−, HER2−, HER1+, and/or CK 5/6+), and
- unclassified, negative for all five markers.

The study also confirms that there are differences in the distribution of breast cancer subtypes by self-declared race. The authors found that 64% of whites had luminal A tumors compared with 48% of blacks. Luminal B disease was found in 11% of whites compared with 8% of blacks. Basal-like tumors were found in 11% of whites and 22% of blacks. HER2+/ER− tumors were seen in 5% of whites and 7% of blacks.

This well-designed study confirms that basal-like breast cancer is associated with a very poor prognosis. In an era before the availability of a drug specific to HER2+ disease, they show that HER2+, ER−, PR− disease was also of similar poor-prognosis.

Although O'Brien et al. report a higher prevalence of basal-like breast cancer in black patients, and especially young black patients, basal-like breast cancer does not appear to be an inherently more aggressive disease in black women compared with white women.

These findings can help us better understand the role of race in breast cancer outcomes. Even though whites historically have had a higher breast cancer incidence rate compared with blacks, breast cancer mortality rates were essentially equal throughout the 1970s. A disparity in mortality was first noted in 1981 (2), with blacks having a higher death rate, and this disparity has been widening ever since (Fig. 1). There was even a small, still unexplained increase in death rate among blacks in the early 1980s. Potential explanations for this black–white disparity include differences in the quality of treatment received by race, and differences in biology by race. Indeed, both likely contribute. Of note, both black and white death rates have been declining since the early 1990s. This is attributed to screening, early detection, and improvements in treatment.

The population-based databases that provided the data in Fig. 1 have not consistently collected tumor marker data. It is known that the beginning of the racial disparities coincided with the availability of tamoxifen, which is active in what is now referred to as luminal A and luminal B disease. The study by O'Brien et al. tells us that these subtypes are more common among white patients.

Many people are not fully comfortable with the use of race in health statistics. The anthropology community insists that race is a sociopolitical and not a biological categorization. In this study, race may be more of a categorization by geographic area of origin. There are known differences in genetic markers among populations as defined by their geographic area of origin. For example, the sickle cell mutation is found in people originating in a contiguous area surrounding the Mediterranean, including Spain, Italy, Greece, the Middle East, and sub-Saharan Africa. There is a higher prevalence of the mutation in sub-Saharan Africa, but it is also prevalent among people who would be considered white from Spain, Italy, and Greece. This example shows that geographic area of origin can be distinctly different from race (3).

Author's Affiliation: Office of the Chief Medical Officer, American Cancer Society, and Departments of Hematology and Medical Oncology, Medicine, and Epidemiology, Emory University, Atlanta, Georgia

Corresponding Author: Otis W. Brawley, American Cancer Society Center, 250 Williams Street, Atlanta, GA 30303. Phone: 404–329-7741; Fax: 770–938-9203; E-mail: Otis.Brawley@cancer.org

doi: 10.1158/1078-0432.CCR-10-2541

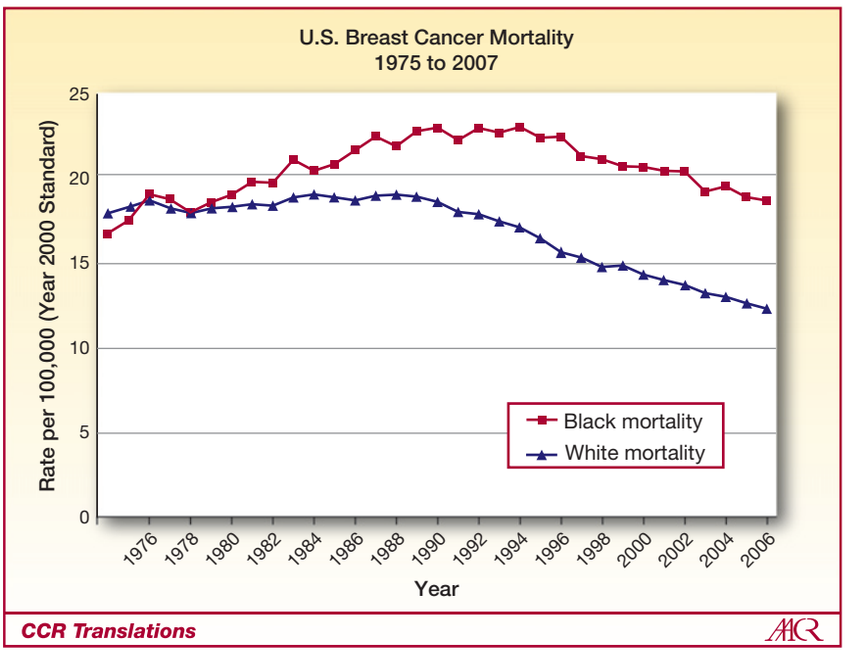

Fig. 1. U.S. SEER Program breast cancer mortality trends from 1975 to 2007 for African-Americans and whites. Data from Altekruse et al. (6).

This study goes a long way toward helping us appropriately define pertinent scientific questions. Although it shows that people of African origin have a higher prevalence of the worst kinds of breast cancer, it also shows that the marker's aggressiveness is more important than race in terms of prognosis. In other words, breast cancer is not a more malignant disease in black women, but a higher proportion of black women get the worst kinds of breast cancer.

In the cohort followed in this study, 29% of black women with premenopausal breast cancer had basal-like disease compared with 15% of white premenopausal women. Why do women of African origin with breast cancer have a higher prevalence of basal cancer? is a very legitimate scientific question. Another interesting question is, Why do a higher proportion of white women have lumina A (ER+) cancer? What is the relationship of these markers with sociopolitical influences such as poverty, diet, body mass index, birthing habits, oral contraceptive use, and postmenopausal hormone replacement?

The role of extrinsic influences on these pathologic markers needs to be further explored. Geographic area of origin can also relate to cultural, social, and economic influences that may influence breast cancer presentation. Indeed, in a study of an all-white cohort in Scotland, Thomson and colleagues (4) suggested that a lifelong history of poverty is correlated with a higher risk of estrogen receptor–negative breast cancer. Gordon (5) reported a similar finding in a United States population.

The article by O'Brien et al. also helps us better understand that there are various kinds of breast cancer. It is very likely that more markers of biological behavior and more targets for treatment will be found in the near future. This will allow for the development of therapies tailored to specific patients. Eventually, we may see genomic definitions for specific cancers with diverse prognoses; indeed, this is the promise of personalized medicine.

In this study, the authors were unable to assess socioeconomic status, body mass index, or treatment patterns. Although this is unfortunate, the article gives us a tremendous amount of information about breast cancer and disparities in the United States. Race can be used as a factor in a sort of benevolent "medical racial profiling," predicting for a higher risk of a worse-prognosis breast cancer. However, once the status of the five markers has been established, race in and of itself should matter little in terms of prognosis.

As we learn to categorize tumors using biological markers, we are also learning that no population has a monopoly on any specific subtype.

Although race should not matter after diagnosis, as the authors appropriately note, race does matter. Issues involving racial differences in breast cancer treatment and access to care continue to drive many of the disparities in outcome.

Received 10/06/2010; accepted 10/29/2010; published online 12/15/2010.

References

1. O'Brien KM, Cole SR, Tse C,et al. Intrinsic breast tumor subtypes, race, and long-term survival in the Carolina Breast Cancer Study. Clin Cancer Res 2010;16:6100–10.

2. Goldson A, Henschke U, Leffall LD, Schneider RL. Is there a genetic basis for the differences in cancer incidence between Afro-Americans and Euro-Americans?J Natl Med Assoc 1981;73:701–6.

3. Brawley OW. Population categorization and cancer statistics. Cancer Metastasis Rev 2003;22:11–19. Brawley OW. Some perspective on black-white cancer statistics. CA Cancer J Clin 2002;52:322–5.
4. Thomson CS, Hole DJ, Twelves CJ, Brewster DH, Black RJ; Scottish Cancer Therapy Network. Prognostic factors in women with breast cancer: distribution by socioeconomic status and effect on differences in survival. J Epidemiol Community Health 2001;55:308–15.
5. Gordon NH. Socioeconomic factors and breast cancer in black and white Americans. Cancer Metastasis Rev 2003;22:55–65.
6. Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W. SEER Cancer Statistics Review, 1975–2007, National Cancer Institute, Bethesda, MD; 2010 [cited 2010 Oct 6]. Available from: http://seer.cancer.gov/csr/1975_2007/.

Clinical Cancer Research

Toward a Better Understanding of Race and Cancer

Otis W. Brawley

Clin Cancer Res 2010;16:5920-5922.