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Editorial

Genetic Testing May Help Reduce Breast Cancer Disparities for African American Women

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Disparities in breast cancer mortality for African American (AA) women are persistent and growing (1). AA women have 42% higher breast cancer mortality than white women, despite having lower disease incidence, and are more likely to be diagnosed with triple-negative breast cancer, which has poorer prognosis than other molecular subtypes (2). Although testing for *BRCA1/2* mutations has been available since the 1990s, more recently testing for panels of multiple high and moderate penetrance genes simultaneously has become common. Chronic underrepresentation of AA women in breast cancer genetic studies has led to uncertainty about both the prevalence of mutations and the risk conferred by mutations among AA women. The study by Palmer et al. (3) in this issue of the Journal is a very important step toward building the evidence base to motivate and guide breast cancer genetic testing among AA women.

Palmer et al. (3) evaluated the associations between mutations in 23 cancer predisposition genes and breast cancer risk among more than 5000 AA breast cancer cases and nearly 5000 AA controls. Mutations were discovered among 8.2% of breast cancer cases and 2.3% of controls. Among women with estrogen receptor (ER) negative disease, 10.8% tested positive. Mutations in *BRCA1*, *BRCA2*, *PALB2*, *CHEK2*, *ERCC3*, and *RECQL* were associated with cancer risk overall, and *BRCA1/2*, *PALB2*, and *RAD51D* were with associated with risk of ER-negative disease. Although this is the largest study to date of genetic predisposition for breast cancer in AA women, the sample sizes for individual genes were small, leading to wide confidence intervals, and therefore future studies need to confirm the results. In addition, the study combined several case-control, cohort, and case-only studies, some of which selected participants based on family history or young age at cancer diagnosis, and therefore mutation prevalence and risk estimates may differ from the general population. Despite these minor limitations, the results strongly demonstrate the value of genetic testing for AA women.

These findings reiterate the pressing need to remove barriers to genetic testing among AA women, including barriers created by stringent and opaque guidelines for testing. In addition to patient-level characteristics such as education and income, prior research shows that physician recommendation is a very strong predictor of genetic testing (4). Current National Comprehensive Cancer Network genetic testing guidelines (5) are complex, with test criteria considering number of affected family members, ages at diagnoses, and tumor characteristics. Implementing such detailed family history assessment has proven challenging, given time constraints in clinical settings and lack of accessible risk assessment tools, with numerous studies showing poor uptake of genetic testing among eligible women (4,6–9), even among those with insurance coverage for genetic testing (8). In this study, the mutation prevalence was 7.2% in cases and 2.2% in controls among women with no first-degree family history compared with 12.4% in cases and 3.2% in controls with a first-degree family history. Most of the mutations (385 of the 530 detected) occurred among women with no first-degree family history. Although information beyond first-degree relatives was not reported, the results suggest that existing family history–based criteria for genetic testing may miss a substantial number of AA mutation carriers. As sequencing costs decrease, testing criteria should be reevaluated and insurance coverage expanded in order to identify mutation carriers early so they can take steps to prevent breast and ovarian cancers.

Second, racial differences in breast cancer biology have important implications for the risk benefit ratios of genetic testing and preventive interventions. To reduce the mortality disparity for AA women, we need to shift focus from identifying risk of cancer overall to identifying risk of ER-negative disease. Women at high risk of triple-negative disease have the most to gain from risk reduction strategies, because it tends to be diagnosed at younger ages, has aggressive tumor characteristics, and treatment options are limited. The value of testing for *PALB2*, for example, is increased because it confers high risk of ER-negative disease, even if the penetrance and prevalence of *PALB2* are lower than *BRCA1/2*. We also need to improve our understanding of the etiology of breast cancer disparities. Given the smaller proportion of ER-negative relative to ER-positive breast cancers and the fact that AA women have been

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underrepresented in genetics research, it is possible that as yet unidentified genetic and nongenetic risk factors as well as gene–environment interactions may contribute to the higher burden of ER-negative disease among AA women. Better understanding of the interplay of genetic and nongenetic risk factors for breast cancer overall as well as for ER-negative tumors would improve risk assessment and aid in directing preventive interventions to AA women at highest risk of dying from breast cancer.

Third, this study provides useful risk estimates that will help guide translation of genetic knowledge to interventions to reduce mortality disparities for AA women. Although prophylactic surgeries, intensive screening, and chemoprevention are recommended for BRCA carriers, there is limited evidence to guide management of non-BRCA mutation carriers. Moderate penetrance mutations may not warrant prophylactic mastectomy, however, breast MRI screening, which has greater sensitivity than mammography (10), may be warranted. Recent trial results highlight the potential of abbreviated breast MRI protocols, which have similar sensitivity to full breast MRI but reduced imaging time and costs (10), for screening women with dense breasts (11,12). Abbreviated breast MRI may be a useful tool for screening non-BRCA mutation carriers, and trials evaluating new imaging and other preventive interventions for high-risk women should be prioritized and performed in diverse populations.

In summary, the study by Palmer et al. (3) highlights the potential value of genetic testing for reducing breast cancer mortality among AA women. Research priorities moving forward include redesigning implementation of genetic testing with emphasis on equitable access to testing for all patients, improving our understanding of genetic and nongenetic risk factors for ER-negative breast cancer, and understanding how to translate this knowledge into effective strategies to reduce breast cancer mortality among AA women.

Note

The authors have no conflicts of interest to disclose.

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