The Time for Mainstreaming Germline Testing for Patients With Breast Cancer Is Now

TO THE EDITOR:

With the cloning of *BRCA1/2* and its functional characterization, we advocated for increased *BRCA1/2* testing to improve prevention and the early detection of breast cancer.[1] More than two decades later, nearly two thirds of patients with breast cancer who are eligible for genetic testing by National Comprehensive Cancer Network (NCCN) guidelines never discuss testing with a health care provider.[2,3] Beitsch et al[4] found no significant difference in pathogenic/likely pathogenic variants among patients with breast cancer who met and did not meet NCCN guidelines for germline genetic testing. Whereas the editorial by Milliron and Griggs[5] offers legitimate concerns about accessibility and inequality with broadened testing, germline testing that is driven primarily by motivated patients and often in a treatment context represents a colossal failure given our ability to prevent the disease in at-risk individuals. We firmly advocate that now is the time to mainstream germline testing for patients with breast cancer and extend cascade testing to all healthy at-risk relatives.

Current NCCN guidelines recommend germline testing for subgroups of patients with breast cancer on the basis of age, triple-negative disease, family history, and Ashkenazi Jewish ancestry.[6] Guidelines are supported by population-prevalence data, but are ultimately expert created. Research during the past decade, however, uncovers a significant burden of preventable inherited breast cancer in diverse populations, including in low- and middle-income countries, such as Nigeria.[7] Narrower guidelines that prioritize patients who are most likely to benefit from genetic testing were reasonable in the 1990s. Today, the lowered costs of genomic testing—as low as $250 for multigene panel testing with coverage often available through health insurance—facilitate expansion. Rather, one of the major remaining barriers is the lack of consistent adoption and knowledge of genetic management across diverse practice settings.[8]

Expanding the use of germline testing for the early detection and prevention of breast cancer requires a more scalable and integrated multidisciplinary approach. As Milliron and Griggs note, with fewer than 700 cancer-specific genetic counselors in the United States, the dependence of the current system on referrals and genetic counseling visits for all germline testing is not sustainable.[5] We have previously described an oncologist-driven approach for genetic counseling in the context of hereditary variants identified using somatic testing. This can be integrated with germline testing in a health system that provides care across the cancer care continuum.[9] Providers can offer genomic testing at the point of care with brief counseling by the physician or midlevel provider regarding possible additional evaluation by a cancer genetics expert. Coupled somatic-germline testing allows for clear assessment of tumor-germline interplay, which limits unnecessary referrals to counselors for possible germline events, as currently experienced with somatic-only testing.[9] Patients with cancer with positive germline results, challenging decision making, or large families that require cascade testing can undergo interdisciplinary counseling with their oncology teams and a genetic counselor in the post-test setting. This approach not only encourages increased genetic literacy among oncologists on both hereditary and somatic levels, but also facilitates the increasing development of experts with dual specialization in clinical oncology and genetics to navigate more complex cases. Basic knowledge of cancer genetics and its implications for management should be an ongoing requirement for oncology certification as we advance novel interventions by which we optimize treatment and reduce financial toxicities.

For healthy at-risk relatives of patients with cancer, the clinical utility of genetic testing not only for inherited breast cancer but also inherited ovarian, prostate, and colorectal cancer is no longer debatable. The benefits of testing are increasingly clear, even for healthy individuals in the general population. Genetic literacy must extend beyond the oncologist to where these patients are: primary care settings, breast centers, colonoscopy suites, and survivorship programs. Removing barriers to testing will increase provider discussion/referral, reduce the financial and time burdens associated with testing, and begin to optimize preventative care for at-risk individuals.[10]

Expanding guidelines will also strengthen advocacy for better management of at-risk populations and access to quality cancer genetic services. Global movements to characterize variants in diverse populations will resolve the questions of variants of unknown significance and moderate-penetrance genes.[5] It is precisely large-scale testing in diverse patient populations that will lead to the improved clinical actionability of findings.

The massive scale of early detection and prevention of breast and other cancers that is possible through the kind of large-scale genetic testing only recently available, coupled with the demonstrated limited

efficacy of existing guidelines, should drive broader genetic testing. However, this is only possible if we embrace a multidisciplinary approach that prioritizes actionable prevention. This mission is shared not only by cancer geneticists but also by oncologists, patients with cancer, and healthy at-risk family members. We can no longer wait for a future with enough genetic counselors to test broadly.

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