Rates of Testing for \textit{BRCA} Mutations in Young Women Are on the Rise

There is a reservoir of patients who should still be tested and we have to figure out how to get to them.

—Jeffrey Weitzel, MD

A recent study has shown that the percentage of young patients with breast cancer who undergo genetic testing for \textit{BRCA} mutations is increasing, in keeping with current guidelines (\textit{JAMA Oncol} [published online ahead of print February 11, 2016]. doi: 10.1001/jamaoncol.2015.5941). The current National Comprehensive Cancer Network guidelines recommend that all women who are diagnosed with breast cancer at aged 45 years or younger be considered for \textit{BRCA} testing, even in the absence of any other risk factors. Underuse of genetic testing in younger women with breast cancer has been demonstrated in previous studies, and the authors of this report set out to describe the frequency of \textit{BRCA} testing in young patients with breast cancer and to characterize how testing results were used in treatment planning.

"Young women who are diagnosed with breast cancer should be counseled to undergo genetic testing, so the fact that we found a trend of increased \textit{BRCA} testing in our cohort in recent years indicates patients (and their providers) are following recommendations," says lead author Shoshana Rosenberg, ScD, MPH, a researcher at the Susan F. Smith Center for Women’s Cancers and an instructor at the Dana-Farber Cancer Institute, both in Boston, Massachusetts.

\textbf{Study Details}

The study by Dr. Rosenberg and her colleagues evaluated women participating in The Young Women’s Breast Cancer Study (YWS). The YWS is an ongoing, multicenter, prospective cohort study established to examine biological, medical, and quality-of-life issues in young women diagnosed with breast cancer at aged 40 years and younger. After enrollment, women were sent a baseline survey followed by additional surveys twice a year for 3 years and annually thereafter. As of December 2014, a total of 1126 women were enrolled in the YWS main study.

To conduct the analysis for their recent study, the authors examined a subset of women from the main YWS cohort. This subset included those women who completed the survey given to them 1 year after study entry and reported on that survey whether they had undergone \textit{BRCA} testing.

The majority of the participants (85%) had at least a college education and 99% were insured. Approximately 87% of the women reported on the 1-year postdiagnosis survey that they had been tested for a \textit{BRCA} mutation. The percentage of women who reported being tested increased from a low of 70% in 2007 to 96% in 2012 and 95% in 2013. Among 780 women tested, 59 (7.6%) were positive for a \textit{BRCA1} mutation, 35 (4.5%) tested positive for a \textit{BRCA2} mutation, 35 (4.5%) had an indeterminate result, and 17 (2.2%) were unsure of the results. The remaining 634 women had a negative test.

Among the 754 women who responded regarding the timing of the return of their \textit{BRCA} results, 277 women (36.7%) said they received their results less than 1 month after diagnosis, 339 women (45%) received them 1 to 3 months after diagnosis, and 78 women (10.3%) received them 3 to 6 months after diagnosis.

In all, 117 women did not undergo genetic testing, and of these, 80 (68%) did speak to their physician or a genetic counselor regarding the risk of having a \textit{BRCA} mutation. Nearly 25% of women said they were not tested because they did not believe they were at risk of having a \textit{BRCA} mutation. Another 25% of women said that they did not undergo the test because their physician did not believe they were at risk. Other reasons for not being tested were genetic testing was not a priority, concerns about insurance or work matters related to harboring a \textit{BRCA} mutation, and the high price

\textbf{KEY POINTS}

\begin{itemize}
  \item Genetic testing for \textit{BRCA} mutations is increasing for young women, which is in keeping with current guidelines, and frequently affects treatment decisions.
  \item Adequate genetic counseling must be widely available for young women with breast cancer.
\end{itemize}
of testing. Approximately one-third of the women who were not tested said they were considering doing so in the future.

“I think the fact that we saw this trend of increased BRCA testing is reassuring, especially in the most recent years, with the caveat that our study population is not necessarily representative of the general US population, since many of the women who are part of our cohort were treated in academic cancer center settings and almost everyone was insured,” says Dr. Rosenberg.

Ann Partridge, MD, MPH, senior author and director of the Program for Young Women with Breast Cancer and senior physician at the Dana-Farber Cancer Institute agreed that the increased rate of testing was positive. However, she says more work is needed. “We need to support these women both emotionally and scientifically as they make decisions about treatment, prevention, and screening in light of information gleaned and limitations of those tests,” Dr. Partridge says. “We also need to examine why some young women still are not being tested and barriers that may be preventing testing and appropriate subsequent care and counseling.”

Impact of BRCA Testing
In all, 248 of 831 women tested (30%) said that the positive or negative result affected their treatment decision: 1) significantly more women who tested positive underwent bilateral mastectomy (86%) than those who tested negative (51%); and 2) they also underwent oophorectomy more frequently if a mutation was present (53% of BRCA mutation carriers vs 2.5% of noncarriers).

Genetic test results did not appear to have any influence on decisions regarding chemotherapy or endocrine therapy.

“It is concerning that 51% choose bilateral mastectomy despite negative testing,” says Jeffrey Weitzel, MD, director of the division of clinical cancer genetics in the department of population sciences at the City of Hope Cancer Center in Duarte, California, who was not involved in the study but did coauthor an accompanying editorial (JAMA Oncol [published online ahead of print February 11, 2016]. doi:10.1001/jamaoncol.2015.5975). “Too many women are choosing bilateral mastectomy and this likely is largely due to inadequate training of the practitioner. It has been shown that physician recommendation is the most influential factor for treatment decisions. Further, not all BRCA-positive patients need to have a bilateral mastectomy. It is an option,” Dr. Weitzel says.

Broader Implications
The prevalence of BRCA testing among young women with breast cancer in the current study was 87%, which far exceeds the prevalence reported in prior studies of BRCA testing, the highest of which was 34%. The authors of the current study say they believe this high rate reflects the fact that the majority of participants were highly educated, insured, and treated in an academic setting, in which genetic counseling and testing are easily accessible.

“The results are encouraging, but more work examining genetic testing in a broader population to address disparities is needed,” says Dr. Weitzel. “Further, this study does not address the women out in the community who should have been tested at diagnosis but were not. There is a reservoir of patients who should still be tested and we have to figure out how to get to them.” Dr. Weitzel says he would also like to know whether the testing of women in the current study was requested by the treating physician, or if the patients underwent genetic counseling.

The researchers plan on including questions on future YWS surveys to assess longer-term outcomes, as well as conducting studies to gain more insight regarding decision making. “As part of a qualitative study focused on how young women make decisions about breast cancer surgery, one theme we are exploring in patient interviews and focus groups is how genetic testing influences choice of surgical treatment,” says Dr. Rosenberg. “We are also asking doctors about their experiences regarding how the presence/absence of a BRCA mutation, along with the more recent availability of testing for hereditary breast cancer genes other than BRCA mutations, affect recommendations about surgery.”

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