Unaffected women and genetic testing for hereditary breast cancer: to test or not to test?

Category II, D: Breast Cancer Genetics/Screening
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Background:
The National Comprehensive Cancer Network (NCCN) guidelines recommend that genetic testing start with a family member affected with cancer, if available. While this process is the most informative, it can be complicated by family dynamics, poor communication, non-testing of affected family members, and other factors. As a result, a growing number of women unaffected with cancer are receiving genetic testing, but little is known about the results of genetic testing in this group. This study aims to describe unaffected women tested with a breast-focused multi-gene panel (MGP) and assessed for meeting NCCN *BRCA1/2* testing criteria.

Methods:
Personal and family history information from females who had either a 6 gene or 17 gene breast-focused MGP between June 2013 and June 2016 were extracted from test request forms and clinic notes and evaluated. Cases with positive results were assessed for meeting NCCN *BRCA1/2* testing criteria.

Results:
Of 21,057 women tested with a 6 gene MGP, 26.0% were unaffected, and 2.9% (n=156) of those unaffected women tested positive for a gene mutation. Of 31,525 women tested with a 17 gene MGP, 21.3% were unaffected, and 5.9% (n=399) of those unaffected women tested positive. Combining positive results for unaffected women from both tests, 507 individuals were assessed using NCCN *BRCA1/2* testing criteria. The majority (91.5%, n=464) of positive, unaffected women met criteria. The vast majority (n=460) met criteria based on family history, while the remaining 4 individuals had a known familial mutation but insufficient family history per our database. Criteria were not met by 8.5% (n=43) of unaffected women with positive results; however, one of these individuals did meet NCCN criteria for Lynch syndrome genetic testing.

Conclusions:
NCCN guidelines recommend increased screening and/or risk reducing measures for women at high risk of developing breast and ovarian cancer due to a germline mutation. However, high risk unaffected women may not be appropriately identified if providers are not utilizing the NCCN criteria to screen their patients. Our data demonstrate that these criteria are able to identify the vast majority of mutation carriers in an unaffected laboratory patient population, and providers should consider utilizing these guidelines to screen their unaffected patients. Additional studies are needed to confirm these results in a broader, clinic-based cohort.