Background and Significance

Approximately 330,000 patients are diagnosed with breast cancer every year in the United States. An estimated 10% of these cancers are likely due to hereditary causes. Studies have estimated that less than 10% of all BRCA1 and BRCA2 carriers will have been identified. Moreover, 50-60% of individuals at risk have not received genetic testing, in part because they do not meet the family history criteria of current testing guidelines and insurance seldom reimburses testing in such cases. An estimated 35,000 breast cancer patients have pathogenic BRCA1/2 variants, yet only 30% have been identified.  

NCCN Guidelines were established in an era when testing was very expensive and known management implications were limited. Today availability of test options has increased, cost of testing has dropped and management guidelines include those relevant to systemic therapy have continued to develop. And yet obstacles including testing guidelines make it challenging to get patients tested and costs covered. We sought to compare PL/P rates in breast cancer patients who met testing guidelines versus those who did not. Our aim was to understand the capability of 2017-2018 NCCN Guidelines to identify breast cancer patients who have variants.

Methods

An IRB-approved multicenter prospective registry was initiated with 20 community and academic breast physicians experienced in genetic testing and management. Sites were selected to help ensure study ethnicity commensurate with United States ethnic demographics.

Eligibility criteria included all breast cancer patients not previously tested. Consecutive patients were consented and underwent an 80 gene test (Invitae–Multi-Cancer Panel). Recruitment goals were 500 patients who meet NCCN genetic guidelines (2017) and 500 who do not. NCCN Guidelines used were 2017-2.

IRB approval and oversight was provided by WRRI (Puyallup, WA) or via a local IRB.

Results

More than 1,000 patients were enrolled and data for 969 subjects were analyzed. 49.99% met NCCN criteria and 50.01% did not.

Variants of uncertain significance (VUS) rates were virtually identical between the two groups.

The overall VUS rate was 54.22% for the entire patient population.

Altogether, almost half of the breast cancer patients tested had either a PL/P variant or a completely negative test with no P, PL, or VUS variants found in 80 genes.

P/LP Variants and NCCN Criteria

Positive Result

BRCA1/2 alone

HBOC “guidelines” panel (11 Genes)

Large Cancer Panel (80 Genes)

In-criteria

2.51%

6.25%

9.39%

Out-of-criteria

0.63%

3.85%

7.92%

Details

• Expanded panel testing yields more pathogenic and likely pathogenic variants than BRCA1 or BRCA2 or Breast Cancer Panels with 11 genes.

• Patients who meet NCCN genetic testing guidelines have similar likelihood of harboring a variant compared to those who do not.

• Universal genetic testing of all breast cancer patients identifies more patients harboring actionable variants than restricting testing to patients who meet NCCN criteria.

• Current testing guidelines if relaxed would increase access to testing for all breast cancer patients including those in low income or other underserved populations.

• Identifying variants in breast cancer patients opens the door for cascade testing of family member opening up true opportunities for prevention or early intervention.

• Existing guidelines for breast cancer patients should be modified to expand testing to all patients offering them additional management options and to open up testing options for family members.

References