Genetic Tests to Identify Risk for Breast Cancer

Julie A. Lynch, Vickie Venne, and Brygida Berse

Objectives: *To describe the currently available genetic tests that identify hereditary risk for breast cancer.*

Data Sources: *Systematic review of scientific literature, clinical practice guidelines, and data published by test manufacturers.*

Conclusion: *Changes in gene patent laws and advances in sequencing technologies have resulted in rapid expansion of genetic testing. While* BRCA1/2 *are the most recognized genes linked to breast cancer, several laboratories now offer multi-gene panels to detect many risk-related mutations.*

Implications for Nursing Practice: *Genetic testing will be increasingly important in the prevention, diagnosis, and treatment of breast cancer. Oncology and advanced practice nurses must understand risk factors, significance of various genetic tests, and patient counseling.*

Key Words: *Breast genetic testing, BRCA, genetic risk, hereditary risk, multigene panels*

Genetic testing has an important role in hereditary risk assessment for breast cancer. There has been rapid expansion of genetic testing as a result of changes in gene patent laws and improvements in gene sequencing technologies. Oncology nurses and advanced practice nurses (APNs) are often asked to educate patients about genetic tests, or may need to assess a patient's family history to determine whether the patient should be referred for genetic counseling. This article provides oncology nurses and APNs with an overview of genetic tests for hereditary mutations that may increase a patient's personal risk of breast cancer or ovarian.

Julie A. Lynch, PhD, RN, MBA: *Veterans Health Administration, Bedford, MA; RTI International, Research Triangle Park, NC; University of Massachusetts Boston, Nursing and Health Sciences, Boston, MA*. Vickie Venne, MS, LGC: *Veterans Health Administration, Salt Lake City, UT*. Brygida Berse, PhD: *Veterans Health Administration, Bedford, MA; RTI International, Research Triangle Park, NC; Boston University School of Medicine, Boston, MA*.

Julie Lynch and Brygida Berse are supported by an interagency agreement from the National Cancer Institute. Veterans Health Administration provides salary support for Julie Lynch and Vickie Venne. The views expressed in this review are those of the authors and do not represent those of the Department of Veterans Affairs, the National Cancer Institute, or the National Institutes of Health.

Address correspondence to Julie A. Lynch, PhD, RN, MBA, Veterans Health Administration, CHOIR, 200 Springs Ave, Bedford, MA 01730. e-mail: julie.lynch@va.gov

Published by Elsevier Inc.
0749-2081/3102-$36.00/0.
http://dx.doi.org/10.1016/j.soncn.2015.02.007

Diagnostic Testing

When reviewing genetic diagnostic testing, it is important to understand the differences between genetic versus genomic testing and germline versus somatic mutations. Generally, a *genetic* test identifies heritable mutations in specific genes, whereas the term *genomic* test usually refers to the analysis of the sequence and/or expression of groups of genes, large fragments of the genome, or even the entire genome. Similarly, the difference between germline and somatic mutations is that a germline mutation is present from the time of conception and, therefore, is carried in all cells of the body and can be passed on to the next generation. An example of a germline mutation is the inherited mutation in the *BRCA1* or *BRCA2* gene. Somatic mutations are acquired during an individual's lifetime through exposure to environmental factors and are usually only present in the tumor. Somatic cancer tests usually require analysis of tumor tissue, whereas germline genetic tests usually analyze a blood sample or a cheek swab.

Mutations that Increase Breast Cancer Risk

The majority of breast cancer patients are the only member of their family with breast cancer and most cases are attributed to environmental or lifestyle factors. Fewer than 15% of women with breast cancer have a first-degree relative with this disease,[1] and only a small fraction of the population carries inherited germline mutations that increase their lifetime cancer risk. Several genes associated with an increased risk of breast cancer have been identified. The level of increased risk and type of cancers that occur in a family will vary with the particular gene involved. Mutations in each gene are rare; however, collectively these mutations account for a significant amount of hereditary cancer susceptibility in the population.

The penetrance of a disease-causing mutation is the likelihood that an individual with the mutation will exhibit clinical symptoms. Mutations in two high-penetrance genes, *BRCA1* and *BRCA2*, account for the majority of hereditary breast cancers and about 5% to 10% of all breast cancers.[2,3] Men and women with harmful *BRCA1/2* mutations are at increased risk of breast cancer development. In addition, *BRCA1/2* mutations account for approximately 15% of ovarian cancers,[4] and these mutations also increase the risk of fallopian tube and prostate cancers. Collectively, the inherited tendency to develop cancers associated with *BRCA1/2* mutations is known as hereditary breast-ovarian cancer (HBOC) syndrome. In addition to these germline mutations, somatic *BRCA1/2* mutations have also been described in ovarian cancer.[5] Mutations in a number of other genes, including *PTEN*, *TP53, STK11, CDH1*, and *PALB2*, have been found to increase the risk of developing breast cancer, although to a lesser extent than *BRCA1/2*.[2,6]

Genetic Testing

Several genetic tests that detect the presence of these cancer-predisposing mutations are commercially available. This type of test involves a blood sample (or a sample of a person's tissue, such as saliva or cheek swab) with DNA analysis for known mutations. Until recently, individual genes were tested separately and sequentially by traditional Sanger sequencing methods. However, decreasing costs and improved efficiencies in high-throughput sequencing technology (next-generation sequencing) have made full gene sequencing and multi-gene panels more cost effective.

The molecular testing landscape is currently in a state of flux. From the late 1990s until 2013, BRCA testing was offered exclusively by Myriad Genetics (Myriad Genetics, Salt Lake City, Utah), a company that patented the *BRCA1* and *BRCA2* genes.[7,8] In June 2013, the US Supreme Court voided Myriad's patents and shortly thereafter several academic and commercial reference laboratories began offering BRCA testing. Examples of academic laboratories that offer BRCA testing include: Baylor College of Medicine, Houston, TX, City of Hope, Duarte, CA, Emory University, Atlanta, GA, Washington University School of Medicine, Saint Louis, MO, Memorial Sloan Kettering, New York, NY, and University of Washington Medical Center, Seattle, WA. Examples of commercial laboratories that offer BRCA testing include: Ambry Genetics, Alisa Viejo, CA, GeneDx, Gaithersburg, MD, Invitae Corporation, San Francisco, CA, Laboratory Corporation of America, Burlington, North Carolina, Myriad Genetics, Quest Diagnostics, Madison, NJ, and Pathway Genomics, San Diego, CA. These laboratories differentiate their services by bundling