Cancer Risks for Men With *BRCA1/2* Mutations

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Testing for mutations in breast cancer genes 1 and 2 (*BRCA1/2*) has been available since 1998, but much of the focus of this testing has been on the implications for women (Weitzel, Blazer, MacDonald, Culver, & Offit, 2011). Women who test positive face a lifetime risk of developing breast cancer of about 87% and about 45% for ovarian cancer, and are confronted with decisions about intensive screening or preventing the malignancies with the use of prophylactic surgery (e.g., bilateral mastectomy, bilateral salpingo-oophorectomy). Women and men who are *BRCA 1/2* positive also may have an increased risk of pancreatic cancer and melanoma. However, the clinical implications for men who carry these mutations are not as clear (Pal et al., 2013).

Background

The *BRCA1/2* mutations are passed to men and women through autosomal dominant transmission. These tumor suppressor genes are located on chromosomes 17q21 and 13q12.3, respectively (Lindor, McMaster, Lindor, & Greene, 2008). Men can pass these genes to both female and male offspring. The clinical implications of men inheriting a mutation are both similar to and different from the implications for women. Those issues need to be considered and discussed with men prior to genetic testing. Limited information currently exists about the cancer risks to men, screening recommendations, and targeted treatment considerations for those diagnosed with malignancy. Men at risk for having a mutation in *BRCA1/2* include those with a known *BRCA1/2* mutation in their family (particularly in first- or second-degree relatives) or men with a family history suggestive of hereditary breast cancer (e.g., a family history of early-onset breast cancer, multiple family members with breast cancer and/or ovarian cancer, being of Ashkenazi Jewish background with a family history of breast or ovarian cancer, a family history of male breast cancer) (Lindor et al., 2008).

Cancer Risks

Men with a mutation in *BRCA1/2* have an increased risk of developing prostate cancer that might be more aggressive, have nodal involvement, and be associated with a poorer survival when compared with men who do not have a mutation (Euhus & Robinson, 2013). Male *BRCA1* carriers may have about twice the risk of developing prostate cancer observed in the general population for men younger than aged 65 years, and *BRCA2* carriers may have five to seven times the risk, based on results from the international research study IMPACT (Identification of Men With a Genetic Predisposition to Prostate Cancer) (Mitra et al., 2011). In another study of 30 patients with prostate cancer with *BRCA2* mutations, those with mutations had a lower mean age at diagnosis (69 years versus 74 years), more advanced tumor stage, higher tumor grade, and a shorter median survival time compared with noncarriers (2.1 years versus 12.4 years) (Tryggvadóttir et al., 2007).

Because the risk of prostate cancer is increased in men with *BRCA* mutations, efforts turn to primary and secondary prevention. The positive predictive value of prostate-specific antigen (PSA) screening might be as high as 47% in men who are *BRCA* positive. The preliminary results from the IMPACT study suggested that screening detects clinically significant prostate cancer (Tryggvadóttir et al., 2007). Those results support the rationale for aggressive screening in this population beginning at age 40 years (instead of beginning at age 50 years for men with the average-population risk) with PSA testing and digital rectal examination (Mitra et al., 2011). The data from the study recommend PSA thresholds of 2.5 ng/ml for men aged 40–49 years, 3.5 ng/ml for men aged 50–59 years, and 4.5 ng/ml in men aged 60–69 years to initiate prostate biopsy with 10 biopsy cores. Early data from the IMPACT study demonstrate that with a PSA threshold of greater than 3 ng/ml, the biopsy rate is 7% with a positive predictive value of 48%. Until final data are available, these data support screening men with known *BRCA* mutations beginning at age 40 years with a PSA threshold for biopsy of 3 ng/ml (Mitra et al., 2011). In comparison, the National Comprehensive Cancer Network ([NCCN], 2012) prostate cancer early detection guidelines suggest that healthcare providers consider a 12-core biopsy for PSA 2.6–4 ng/ml, but recommend a 12-core biopsy for PSA 4 ng/ml or greater for men aged 50 years or older who have average risk.

Lifetime breast cancer risk is estimated at less than 2% for men with *BRCA1* mutations and about 8% for *BRCA2* mutations (Euhus & Robinson, 2013). For all men with breast cancer, poor awareness of the risk of disease and diagnostic delays often result in men being diagnosed with higher-stage tumors and having a poorer overall prognosis (Ruddy & Winer, 2013). It typically presents as a painless subareolar mass. As with women, these men also have an increased risk of pancreatic cancer and melanoma.

Guidelines

Few published guidelines regarding breast cancer screening are available for men, but NCCN (2013) addressed these concerns. Men who are *BRCA* mutation carriers are advised to undergo education regarding breast self-examination, with

a recommendation for regular monthly practice as well as a semiannual clinical breast examination, preferably by a breast surgeon, and prompt evaluation of any suspected breast change (NCCN, 2013). The NCCN (2013) guidelines also recommend a baseline mammogram and annual mammogram if gynecomastia or parenchymal or glandular breast density is identified on baseline study.

Few guidelines exist for prostate screening as well, despite the increased risk for prostate cancer associated with *BRCA* mutations. The NCCN (2013) guidelines recommend that these men consider prostate cancer screening starting at age 40 years.

Other risks may include an increased risk of developing pancreatic cancer; the relative risk may be 2.26–5.9 (Mohamad & Apffelstaedt, 2008), which is three times the estimated risk for pancreatic cancer in the general population. The NCCN (2013) guidelines recommend consideration of pancreatic screening in a research protocol for men and women *BRCA2* mutation carriers.

Both men and women *BRCA* carriers may have an increased risk for developing melanoma; however, the exact risk is not defined. The NCCN (2013) guidelines recommend a full-body skin evaluation for melanoma on an annual basis. An annual ocular evaluation for melanoma is another consideration (Petrucelli, Daly, & Feldman, 2013).

BRCA mutation status may guide the treatment of malignancies, such as male breast cancer or prostate cancer. Preliminary research suggests benefits for targeted treatments in individuals with *BRCA*-associated prostate cancers, including platinum-based treatments and poly(adenosine diphosphate-ribose) polymerase inhibitors (Pal et al., 2013).

Implications for Nurses

The provision of cancer genetics education and counseling services to men with a *BRCA1/2* mutation is important (Shannon & Chittenden, 2012). Data suggest that men from *BRCA* families are interested in pursuing genetic counseling and testing when access is easy, services are free, and a proactive approach is emphasized (Pal et al., 2013). The development of appropriate education and resources focused on *BRCA* mutations in men may enable men who are at high risk for developing these cancers to make informed decisions regarding genetic testing. To date, such materials are extremely limited (Mohamad & Apffelstaedt, 2008).

Educating men about autosomal transmission to offspring is important. An estimated 50% of the population is unaware that breast cancer can be inherited from the father (Shiloh, Dagan, Friedman, Blank, & Friedman, 2013). When a man tests positive, he should be encouraged to share the information with other family members who are potentially at risk, particularly siblings and offspring. Although research is limited, it appears that men who carry a mutation are less likely to have counseling, testing, and participate in the communication of risk information to other family members (Shiloh et al., 2013).

Men also need comprehensive education on cancer risks associated with being a *BRCA* carrier, as well as appropriate screening (Thorne et al., 2011). That would include information about prostate, breast, pancreatic, and melanoma screening both during counseling and in written recommendations.

The psychological implications for men should not be ignored. Similar to women, men who test positive experience stress, anxiety, and possible guilt for transmitting the risk to offspring; men who test negative also may experience survivor guilt, similar to women (Shiloh et al., 2013). They need an opportunity to verbalize these feelings and be provided with concrete strategies to manage their cancer risks.

To date, little research has been completed on the risks and needs of men who carry *BRCA1/2* mutations. A survey of 405 individuals with known *BRCA* mutations (150 men and 232 women) suggested a high interest in more research in this underserved population (Pal et al., 2013). More research needs to be conducted to understand men's needs, which may differ from those of women who are *BRCA* carriers.

Conclusion

As more individuals undergo genetic testing for hereditary cancer syndromes, more men will be identified as *BRCA* mutation carriers. Their needs should not be ignored or underestimated. Oncology nurses can support men as they cope with this information and encourage them to engage in recommended prostate, breast, pancreatic, and melanoma cancer screening as appropriate.

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Genetics & Genomics

This feature aims to educate oncology nurses about the emerging role of genetics and genomics in cancer care. Possible submissions include, but are not limited to, application of genetics and genomics in clinical practice, screening and surveillance, case studies to present new ideas or challenge current notions, and ethical issues. Manuscripts should clearly link the content to the impact on cancer care. Manuscripts should be 1,000–1,500 words, exclusive of tables and figures, and accompanied by a cover letter requesting consideration for this feature. For more information, contact Associate Editor Lisa B. Aiello-Laws, RN, MSN, AOCNS®, APN-C, at lba34@drexel.edu.