EDITORIAL

Prostate, Breast and Ovarian Cancer Genetic Risk Assessment: Connecting the Dots

The pace of understanding the complexities of inherited cancer risk has accelerated since the completion of the Human Genome project in 2003. While most prostate cancers are considered sporadic, up to 15% and possibly more, may be due to the inheritance of specific gene alterations. The classic understanding of hereditary prostate cancer was based on the observation that as the number of first degree relatives with prostate cancer increases so does a man's risk of developing the disease. Subsequently, the increased risk for prostate cancer with a family history of other cancers, such as breast and ovarian cancer, was recognized particularly through inheritance of *BRCA1* or *BRCA2* gene mutations. *BRCA1* and *BRCA2* mutations confer an increased risk for prostate cancer of up to approximately 3-fold and 8-fold, respectively. *BRCA2* mutations have been shown to predispose to early-onset prostate cancer, and aggressive disease. However, the current understanding of genetic testing strategies for inherited breast and ovarian cancer risk in females is better defined and genetic testing experience is far greater than in male patients with prostate cancer.

The 2016 NCCN Guidelines for Genetic/Familial High Risk Assessment of Breast and Ovarian Cancer include prostate cancer in *BRCA1/2* genetic testing criteria.[1] Specifically, females with breast cancer can pursue *BRCA1/2* testing if there are ≥ 2 close blood relatives with prostate cancer with Gleason score ≥ 7. The guideline also includes *BRCA1/2* testing criteria for males, specifically that men with a personal history of prostate cancer (Gleason ≥ 7) with at least one close blood relative with ovarian cancer at any age, breast cancer ≤ 50, or two relatives with breast, pancreatic, or prostate cancer (Gleason ≥ 7) may consider genetic testing. Recommendations for men with *BRCA* mutations to undergo breast examination and prostate cancer screening are addressed in this breast and ovarian cancer guideline. Male *BRCA1/2* mutations carriers are recommended to have self and clinical breast exams starting at age 35. Regarding prostate cancer screening, *BRCA2* mutation carriers are recommended to begin prostate cancer screening at age 40, and *BRCA1* carriers are suggested to follow the same strategy. Current NCCN guidelines for Prostate Cancer Early Detection cross reference the Genetic/Familial High Risk Assessment of Breast and Ovarian Cancer which causes health care professionals to address *BRCA1/2* genetic testing practices for prostate cancer by referencing guidelines for breast and ovarian cancer.[2]

Several major ongoing studies will help clarify the role for genetic testing and counseling for prostate cancer risk such as the US-based Genetic Evaluation of Men (GEM) study and the IMPACT trial based in Great Britain. The IMPACT trial is investigating targeted prostate cancer screening in the context of *BRCA1/2* mutation status. GEM is studying the role of multigene panel testing in men diagnosed with and at increased risk for prostate cancer.

There is much more work to be done to define genetic testing strategies for prostate cancer and to unravel the genetic complexity of this disease through clinical testing. Current genetic testing recommendations for prostate cancer are emerging from breast and ovarian cancer guidelines. Comprehensive genetic testing strategies for men with prostate cancer to assess inherited risk are needed, and will be informed by emerging knowledge of the genetic contribution to prostate cancer. As our knowledge base concerning the genetic basis of inherited disease increases, it will allow information to flow more freely in these disease states and allow us to connect the dots between these and other potentially inherited cancers.

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1. NCCN Guidelines for Genetic/Familial High Risk Assessment of Breast and Ovarian Cancer. Available at www.nccn.org (Accessed September 2016).
2. NCCN Guidelines for Prostate Cancer Early Detection Available at www.nccn.org (Accessed September 2016).