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Gender Disparity: Overlooking Hereditary Prostate Cancer and Implications for Urology Practice

Lauren Bowling, Carin Espenschied, Michelle Jackson, Bryan Mak, Holly Laduca, Aliso Viejo, CA*

INTRODUCTION AND OBJECTIVES: Men and women are equally likely to carry mutations in hereditary cancer genes and both have elevated cancer risks. Prostate cancer (PC) has been associated with germline mutations in several genes, especially BRCA2; which has also been associated with more aggressive disease with significantly lower cause-specific survival. The National Comprehensive Cancer Network (NCCN) guidelines for hereditary breast and ovarian cancer (HBOC) recommend genetic testing for men with a personal and/or family history of high Gleason score prostate cancer with family history of breast, ovarian, and/or pancreatic cancer. Despite this, over 95% of patients who have hereditary cancer multi-gene panel testing (MGPT) are women. We sought to describe results of MGPT in men with PC compared to women with breast cancer (BC).

METHODS: Test results were reviewed for PC patients and female BC patients who had MGPT (Jun 2013 - May 2016) for up to 49 genes. Clinical history was obtained from test request forms.

RESULTS: Of 654 PC probands tested, 100 mutations were identified across 18 genes; 7 individuals had 2 mutations, 93 individuals had 1 mutation. 14.2% (93/654) of PC probands tested positive, compared to only 8.6% of women with BC (6,215/71,728; p=2.5e-5). Most mutations in PC patients were in BRCA (40.9%), followed by ATM (20.4%), CHEK2 (15.0%) and Lynch syndrome-associated genes (9.7%). Of 100 total mutations, 94% were in genes that would impact management recommendations for them and/or their relatives.

The median time from PC diagnosis to MGPT was 6 years, compared to 1 year for female BC. Nearly 57% (53/93) of mutation-positive men had multiple primary cancers, 79.2% of which had PC first. Of BRCA positives with multiple primaries (n=21), over 90% developed PC followed by subsequent cancers, yet testing was not initiated until another cancer developed.

CONCLUSIONS: MGPT identified germline mutations at significantly higher rates in this cohort of men with PC compared to women with BC. Furthermore, 59.1% (55/93) of mutation-positive PC probands had a mutation in BRCA and/or ATM, making them possibly eligible for a PARP-inhibitor clinical trial. Unfortunately, time from PC diagnosis to MGPT was several years longer than women, allowing many to develop subsequent cancers that may have been prevented or detected earlier with knowledge of the germline mutation. Revisions to NCCN guidelines do increasingly recognize the contribution of PC to HBOC; however, increased awareness among clinicians is needed to identify otherwise unrecognized male mutation carriers for appropriate cancer risk management.

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