Are Gleason Score and Metastatic Disease Status Important for Men with Prostate Cancer Undergoing Multigene Panel Testing?
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INTRODUCTION AND OBJECTIVES: Several factors such as age of diagnosis and family history may impact the likelihood of an underlying hereditary predisposition to prostate cancer. Gleason score (GS) and metastatic disease (M+) are prognostic factors in men with prostate cancer. It has been previously reported that men with BRCA1/2 germline mutations have higher GS and typically more aggressive disease than non-BRCA carriers. This study aims to assess if men with mutations in non-BRCA genes have more aggressive disease and/or higher GS, as has been previously described for BRCA1/2, since this may impact treatment planning for these patients.

METHODS: Clinical histories and molecular results for 157 patients tested with a prostate-specific multigene panel test from September 2016-March 2017 were retrospectively reviewed. Patients without a diagnosis of prostate cancer were excluded. The average Gleason score was calculated for all genes that had 2 or more scores available.

RESULTS: Germline mutations were detected in 13.4% (22/157) of patients tested. Mutations were identified in BRCA2 (38%), HOXB13 (19%), ATM (14%), CHEK2 (14%), PALB2 (5%), BRCA1 (5%), and NBN (5%). The median and average age of diagnosis is 55 years old (range: 38-70). Overall, a mean GS of 8 (N=18) and M+ in 38% (N=8) were reported. The average GS was highest for BRCA1/2 (8.86), followed by ATM (7.67), CHEK2 (6.50), and HOXB13 (6.50). Metastatic status was confirmed in 1 ATM, 1 BRCA1, and 6 BRCA2 mutation carriers. No metastatic disease was confirmed in 1 ATM, 1 BRCA2, 1 CHEK2, 2 HOXB13 mutation carriers.

CONCLUSIONS: Detection rates of hereditary cancer usually range from 5-10%; however the detection rate in this study was greater than 13% which highlights the importance of multigene panel testing for men with prostate cancer. The average GS was found to be highest and M+ was seen in the majority of BRCA1/2 mutation carriers, consistent with previous studies. Interestingly, ATM, CHEK2, and HOXB13 were found to have lower average GS and no M+ was seen in a portion of these mutation carriers as well, compared to BRCA1/2 mutation carriers. The current NCCN® guidelines only account for higher GS seen with BRCA1/2 carriers, therefore other gene mutation carriers may be missed if a multigene panel approach isn't considered. This is the first time average GS and M+ have been assessed for germline mutation carriers, therefore further studies are needed to examine these factors in larger populations to draw more concrete conclusions.

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