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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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