Genetic risk factors may tailor prostate cancer screening approaches

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Men with a family history of prostate cancer and African-American men are particularly susceptible to the disease, with a twofold to sevenfold increased risk. Assessing risk in these populations has been difficult.

"There have been years of effort to try to identify genes and genetic mutations associated with prostate cancer as there are for breast cancer," said Veda N. Giri, M.D., director of the Prostate Cancer Risk Assessment Program (PRAP) at Fox Chase Cancer Center, Philadelphia. "Prostate cancer is a more genetically complex disease."

Giri and colleagues studied patients who are part of the center's Prostate Cancer Risk Assessment Program, an early detection program for men with a high prostate cancer risk. More than 700 participants are enrolled; 60 percent are African-American.

The investigators evaluated the clinical characteristics of men at high risk for prostate cancer; those who carry five genetic single nucleotide polymorphisms (SNPs) that have been associated with prostate cancer in recent studies. These genetic changes have mostly been reported in predominantly Caucasian populations and are being studied in African-American men as well.

"We are interested in looking at how these genetic risk markers can be used for assessing the risk for prostate cancer in high-risk men," said Giri. "These are men who have not yet developed prostate cancer, such as African-American men and men with family members with the

disease. Can these markers be used as an indicator of upcoming prostate cancer?"

The men enrolled in PRAP are aged 35 to 69 years and meet one of the following criteria: one first-degree relative with prostate cancer or two second-degree relatives with prostate cancer on the same side of the family. The group also includes African-American men with BRCA 1/2 mutations.

Giri and colleagues compared the Caucasian high-risk men in PRAP with a control group, an all-Caucasian set of men who have no family or personal history of the disease. The men in the control group are at low risk for developing prostate cancer. Analysis revealed that while there was an effect found for increased risk for prostate cancer in Caucasian men at high-risk for several of these markers, none of the results were statistically significant. This could be related to the low sample size used in the study. When comparing these five genetic markers in high-risk Caucasian men with men already diagnosed with prostate cancer, the distribution of the markers was similar. This might indicate that these markers are clinically useful in Caucasian men at risk for prostate cancer, although further study is needed.

"When we compared African-American men in PRAP to the high-risk Caucasian men in PRAP, we did find a difference," she said. "African-American men tended to carry more of these genetic risk markers compared to the Caucasian men. Since African-American men carry more of these particular genetic markers, they may be more informative for prostate cancer risk assessment in African-American men."

The researchers then studied how these markers influence time to prostate cancer diagnosis. "We found a trend that African-American men who carried more of these risk markers tended to develop prostate cancer earlier," Giri said. This finding did not reach statistical

significance.

Giri said the take-home message from this study is that genetic markers associated with prostate cancer risk need to be characterized in prospective screening populations in order to determine how to incorporate them into risk assessment for prostate cancer, particularly for men at high-risk for the disease. "These markers may have significant use in personalizing the early detection of prostate cancer in men at high-risk in order to provide tailored recommendations for screening and diagnosis of this disease," said Giri.

Source: American Association for Cancer Research