Genetic Risk Score Could Identify Men With High-Risk Prostate Cancer

Study confirms that Black men are at higher risk for prostate cancer disease progression and death.

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A scoring algorithm that incorporates 290 different genetic variants associated with prostate cancer could help identify people with a high or low lifetime risk for disease progression or death, which could inform screening decisions, according to a study presented last week at the 2022 ASCO Genitourinary Cancers Symposium.

“Current prostate cancer screening recommendations rely on family history as well as race and ethnicity, factors which often don’t fully capture a person’s risk of developing or dying from prostate cancer,” Robert Dreicer, MD, of the University of Virginia Cancer Center, said in an American Society of Clinical Oncology press release. “This new study suggests that an extensive genetic risk score could be an effective tool to guide screening decisions by identifying people at high or low risk of developing metastatic prostate cancer.”

Prostate cancer is the most common cancer (after noninvasive skin cancer) among men in the United States. However, it often grows slowly, and only a small proportion of men who develop this malignancy will die from it.

Prostate cancer can be detected by a blood test that measures prostate-specific antigen (PSA), a protein produced by the prostate gland. PSA screening can reveal high-risk prostate cancer early, allowing for more effective treatment; reduced screening has been linked to disease progression and higher mortality. On the other hand, screening can also detect low-risk cancer than never would have progressed, resulting in “overtreatment” that can lead to side effects including urinary incontinence and erectile dysfunction.

As such, there is ongoing controversy about the benefits of routine PSA screening. The U.S. Preventive Services Task Force currently recommends that men ages 55 to 69 should make an individual decision in consultation with their doctor, taking into account their specific risk factors and personal preferences; screening is not recommended for older men. Other experts, however, favor a more aggressive screening approach.

Meghana Pagadala, an MD/PhD candidate at the University of California San Diego, and colleagues

aimed to determine whether a genetic risk score could predict the likelihood of metastatic or fatal prostate cancer in a racially and ethnically diverse population. Such scores could inform screening decisions, which might be especially beneficial for Black men, who have a higher average risk of prostate cancer death, the researchers noted as background.

Pagadala's team analyzed data from the Million Veteran Program, a national research initiative to learn how genetics, lifestyle and military exposures affect health and illness among individuals receiving care through the Veterans Health Administration.

The researchers used genotype data to calculate a genetic risk score dubbed PHS290, focusing on 290 previously identified gene variants associated with prostate cancer risk. They also looked at family history of prostate cancer in a first-degree relative (parent, sibling or child), genetic ancestry and self-identified race/ethnicity.

The analysis included nearly 600,000 MVP participants with a median age of 69 years at last follow-up. About 425,000 had European ancestry and about 105,000 had African ancestry, with smaller numbers having Asian or Hispanic/Latino heritage.

Men with PHS290 risk scores in the highest 20% were 4.41 times more likely to die of prostate cancer than those with scores in the lowest 20%. In addition, the risk of developing prostate cancer was 5.66 times greater and the risk of progression to metastatic cancer was 4.18 times greater for men in the top 20%.

Based on these scores, men of African ancestry had the highest risk of disease progression or death, being 1.84 time more likely to develop prostate cancer, 2.27 times more likely to progress to metastatic cancer and 1.97 times more likely to die compared with white men. Hispanic/Latino men had risk levels similar to those of white men. The study did not include enough Asian men to come up with reliable risk estimates for this group.

While people with a family history of the malignancy also had a higher risk of developing and dying from prostate cancer, the PHS290 risk score remained a strong independent predictor of fatal prostate cancer even after taking family history and ancestry in account.

An advantage of this algorithm is that it incorporates nearly 300 gene variants, whereas some available commercial tests use only a dozen or so genes, Pagadala noted. What's more, this genetic information does not change over a person's lifetime, while tumor characteristics can change, and tumor genomic testing can only be done after a person has already developed cancer.

"While most prior genetic studies have focused on men of European ancestry, our scoring algorithm is a measure of risk of dying of prostate cancer in a diverse population of military veterans," Pagadala said. "Even accounting for family history and ancestry, the scoring algorithm provided powerful additional information about a man's risk of death due to prostate cancer."

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