Joint Biochemical & Genetic Prostate Cancer Risk Stratification

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ABSTRACT

Background and Objective: Overdiagnosis of prostate cancer (PC) through prostate-specific antigen (PSA) testing at short intervals remains common. While baseline serum PSA abundance < 1 ng/mL warrants infrequent screening, it is critical to foster advanced diagnostic practices for men with baseline serum PSA ≥ 1 ng/mL, who are at higher risk for clinically significant disease. We investigated whether common germline variants could enhance screening recommendations in men with PSA ≥1 ng/mL.

Methods: Polygenic hazard scores for the risk of prostate cancer diagnosis (PHS290) were computed in a diverse, matched, prospective cohort of 310 men with baseline PSA ≥ 1 ng/mL with or without PC. Regression models were used to predict prostate cancer clinical risk groups with PHS290, while incorporating clinical covariates.

Key Findings: PHS290 stratified individuals with PSA ≥1 ng/mL into risk groups and identified men with intermediate- & high-risk PC. In a case-control analysis, PHS290 distinguished clinically significant PC from men with low-grade and no prostate cancer combined. In a time-to-event analysis, PHS290 was significantly associated with increased hazard of clinically significant PC.

Conclusions and Clinical Implications: Our study demonstrates the potential of genetic scores to advance screening guidance. The prostate cancer risk stratification capabilities of molecular biomarkers in tiered screening strategies merit further study in large cohorts and incorporation into baseline risk calculators.

Conflicts of Interest:
P.C.B. sits on the Scientific Advisory Boards of BioSymetrics Inc and Intersect Diagnostics Inc., and formerly sat on that of Sage Bionetworks. T.M.S. reports honoraria from Varian Medical Systems, WebMD, GE Healthcare, and Janssen; he has an equity interest in CorTechs Labs, Inc. and serves on its Scientific Advisory Board; he receives research funding from GE Healthcare through the University of California San Diego. These companies might potentially benefit from the research results. The terms of this arrangement have been reviewed and approved by the University of California San Diego in accordance with its conflict-of-interest policies. All other authors declare they have no conflicts of interest.

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