Risk Analysis of Prostate Cancer in PRACTICAL, a Multinational Consortium, Using 25 Known Prostate Cancer Susceptibility Loci.

Abstract:
Genome-wide association studies have identified multiple genetic variants associated with prostate cancer risk which explain a substantial proportion of familial relative risk. These variants can be used to stratify individuals by their risk of prostate cancer. We genotyped 25 prostate cancer susceptibility loci in 40,414 individuals and derived a polygenic risk score (PRS). We estimated empirical odds ratios (OR) for prostate cancer associated with different risk strata defined by PRS and derived age-specific absolute risks of developing prostate cancer by PRS stratum and family history. The prostate cancer risk for men in the top 1% of the PRS distribution was 30.6 (95% CI, 16.4-57.3) fold compared with men in the bottom 1%, and 4.2 (95% CI, 3.2-5.5) fold compared with the median risk. The absolute risk of prostate cancer by age of 85 years was 65.8% for a man with family history in the top 1% of the PRS distribution, compared with 3.7% for a man in the bottom 1%. The PRS was only weakly correlated with serum PSA level (correlation = 0.09). Risk profiling can identify men at substantially increased or reduced risk of prostate cancer. The effect size, measured by OR per unit PRS, was higher in men at younger ages and in men with family history of prostate cancer. Incorporating additional newly identified loci into a PRS should improve the predictive value of risk profiles. We demonstrate that the risk profiling based on SNPs can identify men at substantially increased or reduced risk that could have useful implications for targeted prevention and screening programs.
TUM Einrichtung:
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