

Genetic Variants and Polygenic Risk Score for Predicting Prostate Cancer Aggressiveness

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Background

Prostate cancer (PCa) is the most common malignancy among men, accounting for about 30% of the total cancer cases and ranking second in cancer-related deaths in US men. Some inherited single nucleotide polymorphisms (SNPs) associated with PCa aggressiveness have been reported, but their associations are often weak. Polygenic risk scores (PRSs), which combine multiple SNPs, were published for predicting PCa aggressiveness. One PRS with 290 SNPs, of which 270 are biallelic SNPs (PRS-m270) was shown to significantly predict age at diagnosis of aggressive PCa.

Objectives

This study evaluates PRS-m270 for predicting PCa aggressiveness for patients with self-reported white race.

Method

This study used SNP data from 309 PCa patients with self-reported white race from the archived blood samples at LSUHSC and Moffitt Cancer Center. The prevalence of PCa aggressiveness is ~12%. After quality control procedures, 495,318 SNPs and 305 PCa patients remained. Of the 270 SNPs in PRS-m270, 41 were available in the genotyped data. Logistic regression models are used to assess SNPs (treated as an additive inheritance mode as 0, 1, and 2) and the PRS associated with PCa aggressiveness. These associations will also be tested based on imputed SNP data.

Result

Among the 41 SNPs in PRS-m270 identified in 305 self-reported white patients, 3 SNPs (rs5919393 (AR), rs10993994 (MSMB), & rs3454027 (ADAMTSL1)) were promising ($p < 0.05$) for predicting PCa aggressiveness. The patients with the G allele in each SNP had a significantly higher risk of developing aggressive PCa. However, the combined PRS with 41 SNPs did not significantly predict aggressive PCa, which may be due to many missing values ($n=112$).

Conclusion

Only 15% of the target SNPs were available in the genotyped data, and missing values limited the predictive power of the PRS. Despite this, three SNPs were identified as significant predictors of aggressive PCa among White patients. To improve robustness of PRS, future analyses will incorporate imputed SNP data to better assess the clinical utility of the PRS in predicting PCa aggressiveness.

This study is approved under IRB protocol #5543.