Causal effect of type II diabetes on prostate cancer in the East Asian population: A two-sample Mendelian randomization study

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Introduction

Type II diabetes, a metabolic disease, and prostate cancer are prevalent diseases in the elderly population. Whether type II diabetes has an association with prostate cancer has not been thoroughly studied. Limited research has been performed from a perspective of genetic level, especially among non-European populations. In this study, we used a two-sample Mendelian randomization (MR) approach to evaluate the causal effect between type II diabetes as an exposure and prostate cancer as an outcome in the East Asian population.

Materials and Methods

For type II diabetes, we used 174 risk loci identified in a meta-analysis of 77,418 cases and 356,122 controls from 23 East Asian Genome-wide Association Studies (GWAS). For prostate cancer, summary statistics were extracted from the GWAS from BioBank Japan using 5,408 cases and 103,939 controls. We performed two-sample Mendelian randomization with the inverse variance weighted method while using MR Egger and weighted median methods as sensitivity analysis. For type II diabetes risk SNPs not directly present in the prostate cancer GWAS, we identified proxy SNPs in linkage disequilibrium ($r^2 > 0.8$) using the 1000 genome project. We used *P-value* < 0.05 as a threshold to determine statistical significance.

Figure 1 Comparison of SNP Effects on Prostate Cancer versus Type II Diabetes

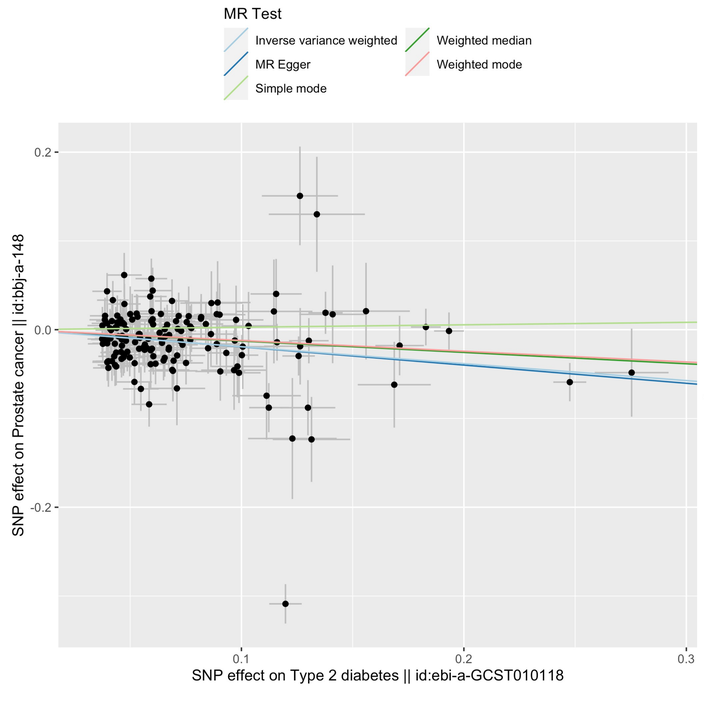
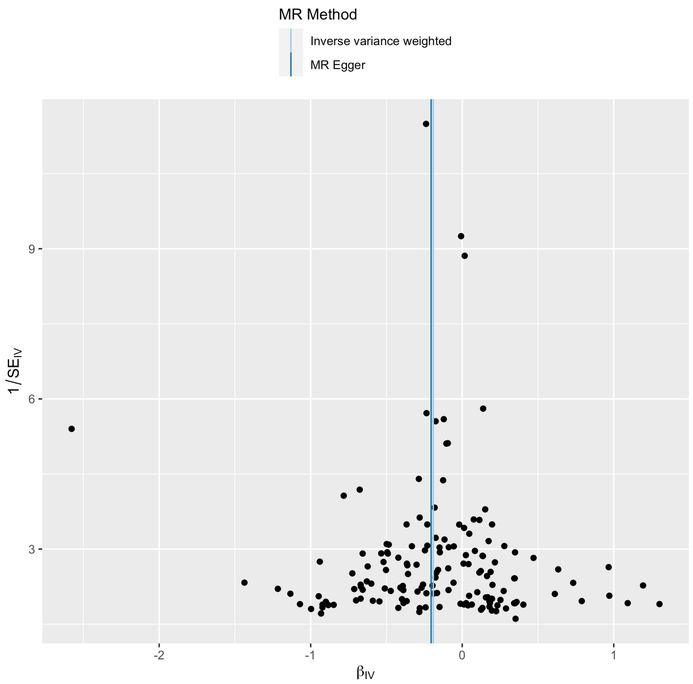


Figure 2 Funnel Plot to Gauging the Reliability of SNP Effects



Conclusion and Discussion

Based on 152 out of 174 SNPs of type II diabetes in the East Asian population, we found that type II diabetes had a significant negative causal effect on prostate cancer [Odds Ratio (OR) = 0.76, 95% Confidence Interval (CI): 0.76 - 0.89, $P = 2.26 \times 10^{-6}$]. Results from sensitivity analysis with other weighting methods provided similar results.

In conclusion, we observed an inverse relationship between type II diabetes and prostate cancer among the East Asian population. Patients with diabetes may have a lower risk of prostate cancer due to a reduced level of insulin and testosterone. To validate this association, further research is needed on those hormones and prostate cancer risk at the metabolic level.

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