Univariable and multivariable two-sample Mendelian randomization investigating the effects of leisure sedentary behavior on the risk of lung cancer

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Background

Leisure Sedentary behaviors (LSB) are widespread and observational studies have provided emerging evidence that LSB plays a role in the development of lung cancer (LC). However, the causal inference between LSB and LC remains unknown.

Methods

We utilized univariable (UVMR) and multivariable two-sample Mendelian randomization (MVMR) analysis to disentangle the effects of LSB on the risk of LC. MR analysis was conducted with genetic variants from genome-wide association studies of LSB (408,815 persons from UK Biobank), containing 152 single nucleotide polymorphisms (SNPs) for television (TV) watching, 37 SNPs for computer use and 4 SNPs for driving, and LC from the International Lung Cancer Consortium (11,348 cases and 15,861 controls). Multiple sensitivity analyses were further performed to verify the causality.

Results

UVMR demonstrated genetically predisposed 1.5 h increase in LSB spent on watching TV increased odds of LC by 90% (odds ratio (OR) 1.90, 95% confidence interval (CI) 1.44-2.50, $P < 0.001$), similar trends were observed for squamous cell lung cancer (OR 1.97, 95%CI 1.31-2.94, $P = 0.0010$) and lung adenocarcinoma (OR 1.64, 95%CI 1.12-2.39, $P = 0.0110$). Causal effects remained to be significant after adjusting for education (OR 1.97, 95%CI 1.44-2.68, $P < 0.001$) and body mass index (OR 1.86, 95%CI 1.36-2.54, $P < 0.001$) through MVMR approach. No association was found between prolonged LSB spent on computer use and driving and LC risk. Genetically predisposed prolonged LSB was additionally correlated with smoking (OR 1.557, 95%CI 1.287-1.884, $P < 0.001$) and alcohol consumption (OR 1.010, 95%CI 1.004-1.016, $P = 0.0016$). Consistency of results across complementary sensitivity MR methods further strengthened the causality.

Conclusions

Robust evidence was demonstrated for an independent, causal effect of LSB spent on watching TV in increasing risk of LC. Further work is necessary to investigate the potential mechanisms.

Disclosure

Conflicts of Interest: The authors have no conflicts of interest to declare.

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