

Associations between Leisure Sedentary Behaviours and Risk of Breast Cancer: A Two-sample Mendelian Randomisation Study

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Introduction: Previous observational studies have shown that leisure sedentary behaviours were associated with breast cancer risk, but whether there are causal relationships remains unknown. This study aimed to explore the potential cause-and-effect associations between leisure sedentary behaviours and risk of breast cancer and its immunohistochemical types by a two-sample Mendelian randomisation (MR) study.

Methods: The summary-level genome-wide association studies data for three leisure sedentary behaviours (television watching, leisure computer use, and driving behaviour) and breast cancer and its immunohistochemical types (estrogen receptor (ER) positive and ER negative breast cancer) were derived from the United Kingdom Biobank and the Breast Cancer Association Consortium, respectively. Single-nucleotide polymorphisms (SNPs) that were significantly associated with the exposures ($P\text{-value} < 1 \times 10^{-8}$) were identified as instrumental variables (IVs). The odds ratios (ORs) and 95% confidence intervals (95% CIs) per one standard deviation (SD) change in the exposures for risk of breast cancer and its subtypes were calculated by the inverse variance weighted method.

Results: We selected 84, 19, and three SNPs as IVs for television watching, leisure computer use, and driving behaviour, respectively. Each SD (1.5 h) increase in television watching time was positively associated with risk of overall breast cancer (OR=1.25, 95% CI=1.08-1.45, $P=0.003$), ER positive breast cancer (OR=1.28, 95% CI=1.08-1.53, $P=0.005$), and ER negative breast cancer (OR=1.30, 95% CI=1.04-1.62, $P=0.020$). However, no associations of leisure computer use and driving behaviour with risk of breast cancer and its subtypes were found.

Conclusions: Leisure sedentary behaviours (especially for television watching) were causally associated with risk of breast cancer and its immunohistochemical types. Our findings highlight the significance of reducing leisure sedentary behaviours in preventing breast cancer. Future MR studies with more and stronger SNPs and external validation of the findings are needed.

Keywords: sedentary behaviour, breast cancer, Mendelian randomisation