A Two-Sample Mendelian Randomization Study of Lifestyle Factors and the Risk of Pancreatic Cancer

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Background : This study aimed to examine the potential causal relationship between lifestyle factors and pancreatic cancer (PC) risk, with the broader goal of informing prevention strategies through modifiable behaviors.

Methods : A two-sample MR analysis was conducted using data from published genome-wide association studies (GWAS) of individuals of European ancestry. The exposures included obesity (body mass index [BMI], waist-to-hip ratio adjusted for BMI [WHRadjBMI]), smoking (smoking status, cigarettes per day), alcohol consumption, and physical activity (moderate-to-vigorous physical activity [MVPA]). PC GWAS data included 663 cases and 410,350 controls from the GWAS Catalog. The primary method was inverse-variance weighted (IVW), with additional analyses using the contamination mixture method, MR-Egger, weighted median, simple mode, and weighted mode approaches. We conducted heterogeneity tests, assessed horizontal pleiotropy, and performed leave-one-out analyses to evaluate the robustness of the results.

Results : Higher WHRadjBMI (OR = 1.84, 95% CI: 1.08–3.16), current smoking (OR = 3.93, 95% CI: 1.11–13.85), and higher cigarettes per day (OR = 3.20, 95% CI: 1.37–7.45) were significantly associated with increased PC risk. Higher MVPA (OR = 0.16, 95% CI: 0.03–0.82) was inversely associated. No significant associations were observed for BMI or alcohol consumption. There was no evidence of heterogeneity and horizontal pleiotropy (all P-values > 0.05).

Conclusion : This MR study supports evidence for a potential causal association between smoking, central adiposity, and increased PC risk, and suggests that MVPA may offer protective effects. These findings highlight the importance of targeting smoking cessation, reducing abdominal obesity, and promoting physical activity in PC prevention efforts. Further studies with larger samples, diverse populations, and advanced methods addressing pleiotropy are warranted to validate and extend these findings.

Early-Life Exposures and Multiple Myeloma Risk: A Population-based Case-Control Study in Australia

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Background : Multiple myeloma (MM) is a hematologic malignancy with few known modifiable risk factors. Emerging evidence suggests that early-life exposures may influence immune system development and, in turn, affect cancer susceptibility. Our aim was to examine whether exposures while in utero or during early childhood were associated with MM risk.

Methods : We conducted a population- and family-based case–control study in Australia, comprising 782 MM cases and 1,121 controls. Early-life exposures including maternal smoking, being breastfed, childhood growth patterns, household living arrangements, and pet ownership were assessed via self-administered questionnaires. Multivariable logistic regression models, adjusted for age at enrolment, sex, country of birth, socioeconomic position, rural-urban residence and birth weight, were fitted using multiple imputation by chained equations (MICE) to handle missing data.

Results : Living in a home with five or more children was associated with a lower risk of MM (OR = 0.58, 95% CI: 0.38–0.87). Sharing a bedroom before age 11 years (OR = 0.80, 95% CI: 0.64–1.00) and pet ownership in early childhood (OR = 0.77, 95% CI: 0.60–0.99) were also inversely associated with MM risk. No clear associations were observed for maternal smoking during pregnancy (OR = 1.10, 95% CI: 0.80–1.52), being breastfed (OR = 1.00, 95% CI: 0.74–1.35), or height relative to peers at age 7 or 11 (7 years: OR=1.10, 95%CI: 0.86-1.41; 11 years: OR=1.05, 95%CI: 0.83-1.33).

Conclusion : Our findings support the hypothesis that early-life immune stimulation through environmental exposures may reduce the risk of MM. Further studies are needed to elucidate the biological mechanisms underlying these associations and to explore potential preventive strategies.

Global trends of early-onset cancers: Comparisons of incidence, mortality, and obesity prevalence

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Background : The rising incidence of early-onset cancers (diagnosed at ages 20-49) is a global public concern. We examined 1) whether the incidence trend of early-onset cancers was higher than that of later-onset cancers (diagnosed at ages ≥50), 2) whether the incidence and mortality of early-onset cancers increased concurrently, and 3) whether the obesity prevalence in younger populations (aged 20-49) was correlated with the early-onset cancer incidence between 2000 and 2017.

Methods : We used age-standardized incidence and mortality rates for early-onset and later-onset cancers in 44 countries from the Cancer Incidence in Five Continents and WHO mortality databases. We retrieved national obesity prevalence data from the National Clinical Database. Average annual percentage changes (AAPCs) for cancer incidence and mortality were calculated by joinpoint regression models. We calculated Spearman's rank correlation coefficient (ρ) as a measure of correlation between the obesity prevalence and cancer incidence.

Results : The following early-onset cancer types had significantly higher AAPCs than later-onset cancer types in females: colorectal cancer (6 countries), cervical cancer (6 countries), pancreatic cancer (5 countries), and multiple myeloma (5 countries); in males: prostate cancer (12 countries), colorectal cancer (8 countries), and kidney cancer (6 countries). Early-onset uterine (5 countries) and colorectal cancer (females: 3 countries, males: 5 countries) showed significantly positive AAPCs in both incidence and mortality. Strong positive correlations were observed between the obesity prevalence and the incidence of early-onset obesity-related cancers in many countries.

Conclusions : Early-onset cancer incidence has more rapidly increased than later-onset cancer incidence and has concurrently increased with mortality for some cancer types. Our study also highlights a significant role of the global obesity epidemic in the early-onset cancer epidemic.

Elevated risk of fractures in Japanese cancer survivors: A 10-year longitudinal study

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Cancer survivors may face increased risk of fragility fractures (FFs) due to treatment-induced bone loss, but longitudinal evidence in Asian populations remains scarce. This study aimed to clarify the risk of FFs in Japanese cancer survivors compared with individuals without cancer by incorporating time-dependent variables. In a 10-year cohort of 10330 Japanese adults aged 40–69 years, we assessed FF (i.e., hip, vertebral compression, and distal radius fractures) risk associated with cancer status using time-dependent Cox proportional hazards analyses, adjusting for age, sex, menopausal status, body mass index, highest educational attainment, number of comorbidities, hormone replacement therapy, osteoporosis medication use, corticosteroid use, smoking status, alcohol drinking, physical activity, and total energy intake. The time-dependent variables included cancer status and age, which changed during the follow-up period. Additionally, the analyses were performed according to cancer treatment status, number of primary cancers, and cancer site. Among 10330 participants (mean age, 56.4 years; female, 6148), 386 participants experienced FFs. Compared with participants without cancer, higher risk of overall FF was observed in participants with cancers (hazard ratio [HR], 1.40; 95% confidence interval [CI], 1.03–1.89). This risk was further elevated among participants with current cancer (HR, 1.71; 95% CI, 1.15–2.55), multiple primary cancer (HR, 1.42; 95% CI, 1.04–1.95), and those with stomach (HR, 1.84; 95% CI, 1.01–3.37), kidney (HR, 3.74; 95% CI, 1.20–11.70), or hematologic cancers (HR, 7.70; 95% CI, 2.45–24.16). By applying time-dependent Cox proportional hazards models to accurately account for changes in cancer status over time, we found that Japanese cancer survivors had higher risks of overall FF compared to those without cancer. These findings highlight the importance of FF prevention strategies in cancer survivorship care in aging Asian populations.