Mendelian randomization study of height and risk of colorectal cancer

Background: For men and women, taller height is associated with increased risk of all cancers combined. For colorectal cancer (CRC), it is unclear whether the differential association of height by sex is real or is due to confounding or bias inherent in observational studies. We performed a Mendelian randomization study to examine the association between height and CRC risk.

Methods: To minimize confounding and bias, we derived a weighted genetic risk score predicting height (using 696 genetic variants associated with height) in 10,226 CRC cases and 10,286 controls. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) for associations between height, genetically predicted height and CRC.

Results: Using conventional methods, increased height (per 10-cm increment) was associated with increased CRC risk (OR = 1.08, 95% CI = 1.02-1.15). In sex-specific analyses, height was associated with CRC risk for women (OR = 1.15, 95% CI = 1.05-1.26), but not men (OR = 0.98, 95% CI = 0.92-1.05). Consistent with these results, carrying greater numbers of (weighted) height-increasing alleles (per 1-unit increase) was associated with higher CRC risk for women and men combined (OR = 1.07, 95% CI = 1.01-1.14) and for women (OR = 1.09, 95% CI = 1.01-1.19). There was weaker evidence of an association for men (OR = 1.05, 95% CI = 0.96-1.15).

Conclusion: We provide evidence for a causal association between height and CRC for women. The CRC-height association for men remains unclear and warrants further investigation in other large studies.

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