

Adiposity, proteins, colorectal cancer: Mendelian randomization analysis

Wednesday, 21 September 2022 12:42 (6 minutes)

Evidence suggests that increased and excess fat mass, adiposity, is associated with increased colorectal cancer risk. There is also evidence that concentrations of many circulating proteins are altered in individuals with adiposity and colorectal cancer. Whether these proteins mediate the association between adiposity and colorectal cancer is not clear.

We use two-sample Mendelian randomization (MR) to assess the potential causal relationship between: (i) adiposity measures (body mass index (BMI), waist hip ratio (WHR), and WHR adjusted for BMI) and overall and site specific colorectal cancer; (ii) adiposity measures and 4,907 proteins; 4,907 proteins and overall and site specific colorectal cancer. We subsequently performed multivariable MR to assess the potential mediating affect of proteins which are associated with both adiposity measures (ii) and colorectal cancer (iii). All analyses were performed using sex-combined and sex-specific data.

Preliminary results of over 500,000 models suggest adiposity measures are associated with over half of the 4,907 proteins and that the majority of these proteins are associated with colorectal cancer. Analyses using cis only SNPs are currently being performed and results will guide the multivariable MR analyses for which results will be available to present at the ECSA day.

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Session Classification: Lightning poster presentation