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Summary

ROLES OF MODIFIABLE RISK FACTORS IN MEDIATING THE CAUSAL EFFECT OF LIVER CIRRHOSIS ON COLORECTAL CANCER: A TWO-STEP MENDELIAN RANDOMIZATION STUDY

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A two-step Mendelian randomization study finds a causal association between genetically predicted liver cirrhosis and increased colorectal cancer risk, with waist-to-hip ratio mediating 7.45% of this effect.

KEY POINTS

- Liver cirrhosis was causally associated with colorectal cancer in inverse variance weighted analysis (OR 1.193, 95% CI 1.008–1.411, p = 0.040).
- Waist-to-hip ratio explained 7.45% of the total effect of cirrhosis on colorectal cancer risk, with a mediation effect estimate of 0.013 (standard error 0.006).
- Multivariate Mendelian randomization identified body mass index, whole body fat mass, waist-to-hip ratio, and alcohol consumption as independent risk factors for colorectal cancer ($p < 0.05$).
- Gene set enrichment analysis identified SERPINE1 and ARKND1 as intersection genes in both liver cirrhosis and colorectal cancer tissues, with potential mechanisms including epithelial-mesenchymal transition, coagulation, and inflammatory response.
- The study used single-nucleotide polymorphisms as instrumental variables with data from FinnGen and other databases to explore causal relationships and modifiable mediators.

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