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Association between pre-diagnostic circulating lipid metabolites and colorectal cancer risk: a nested case-control study in the European Prospective Investigation into Cancer and Nutrition (EPIC)

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Introduction
Lipids are involved in many metabolic processes that may be relevant for cancer development. However, the role of specific lipid metabolites on colorectal cancer risk is unclear.
Methods
In a case-control study nested within the European Prospective Investigation into Cancer and Nutrition (EPIC), we examined associations between pre-diagnostic circulating concentrations of 97 lipid metabolites (acylcarnitines, glycerophospholipids and sphingolipids) and colorectal cancer risk. Circulating lipids were measured using targeted mass spectrometry (Biocrates AbsoluteIDQ Kit) in 1,591 incident colorectal cancer cases and 1,591 matched controls. Multivariable conditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between concentrations of individual lipid metabolites and metabolite patterns with colorectal cancer risk.
Results
Of the 97 assayed lipids, 24 were inversely associated (nominally at $p<0.05$) with colorectal cancer risk. Hydroxysphingomyelin (SM (OH)) C22:2 (ORper doubling 0.60, 95%CI 0.47-0.77) and phosphatidylcholine (PC) ae C34:3 (ORper doubling 0.71, 95%CI 0.59-0.87) remained associated after multiple comparisons correction. These associations were unaltered after excluding cases diagnosed <5 years after blood collection and were consistent according to sex, age at diagnosis, BMI, and colorectal subsite. Associations between metabolite patterns and colorectal cancer risk yielded a similar pattern of results, with inverse associations observed for one component including 26 phosphatidylcholines and all sphingolipids (OR per doubling0.93, 95% CI 0.88-0.99, p=0.0162) and weaker evidence of an inverse association with another component including 30 phosphatidylcholines (OR per doubling 0.95, 95% CI 0.90-1.00, p=0.0529).
Conclusion
Elevated pre-diagnostic circulating levels of SM (OH) C22:2 and PC ae C34:3 and lipid patterns including phosphatidylcholines and sphingolipids were associated with lower colorectal cancer risk. Additional studies are needed to confirm these novel associations and understand the role of lipid dysregulation in colorectal cancer development.

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