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Lifestyle, dietary, and anthropometric correlates of eight circulating metabolites prospectively associated with breast cancer risk in EPIC

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Metabolomics is a promising molecular tool to identify novel etiologic pathways leading to cancer. Using a targeted approach in a prospective setting, we previously identified associations between 8 circulating metabolites (acetylcarnitine (positive association), arginine, asparagine, phosphatidylcholines (PCs) aa C36:3, ae C34:2, ae C36:2, ae C36:3 and ae C38:2 (negative associations)) and risk of breast cancer among women not using hormones at blood collection.

To identify possible novel preventive strategies, we conducted a cross-sectional analysis nested in the EPIC cohort to identify major correlates of circulating concentrations of these metabolites among lifestyle, anthropometric, and dietary factors. This work included 2358 women not using hormones at blood collection, defined as controls in previous case-control studies nested within EPIC, for whom concentrations of the 8 metabolites had been previously measured (AbsoluteIDQ p180 platform, Biocrates Life Sciences, Innsbruck, Austria). Associations of each metabolite concentration with 42 potential correlates were assessed using linear regression models adjusted for potential confounders in a discovery set of 1572 participants. Significant associations after correction of P-values for multiple testing were evaluated using the same models in a validation set of 786 women.

Concentrations of PCs ae C34:2, ae C36:2, ae C36:3 and ae C38:2 showed negative associations with adiposity, and positive associations with total and saturated fat intakes. PC ae C36:2 also showed a negative association with alcohol consumption, and positive associations with the WCRF/AICR lifestyle and the healthy living index scores. Asparagine concentrations were negatively associated with adiposity, and arginine concentrations were not associated to any of the factors examined. Acetylcarnitine concentrations were positively associated with age but with none of the other factors.

These associations bring new insights on possible mechanisms underlying associations between lifestyle and anthropometric factors and risk of breast cancer. Further work is needed to identify potential non-lifestyle correlates of arginine and acetylcarnitine, which could point to novel potential preventive strategies.

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