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Prospective Analysis of Circulating Metabolites

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Perspective

Endometrial cancer is highly linked to obesity, and metabolic dysregulation, such as oestrogen and insulin signalling, is a causative risk factor for the disease. We used metabolomics studies on pre-diagnostic plasma samples from 853 case-control pairs from the European Prospective Investigation into Endometrial Cancer to find new metabolic pathways linked to endometrial cancer.

A brief introduction with over 380,000 new cases identified worldwide in 2018, endometrial cancer is the sixth most frequent cancer among women. Endometrial cancer has been on the rise in recent decades, owing to the obesity epidemic and decreased hysterectomy rates, and this trend is expected to continue in the coming decades are explained by known modifiable and non-modifiable risk factors. The laboratory of Cancer Metabolism and Systems Toxicology (Imperial College London) used a 1290 Agilent UPLC connected to a QTRAP 4000 SCIEX mass spectrometer to conduct targeted metabolomics studies of plasma samples utilising a liquid chromatography-tandem mass spectrometry (LC-MS/MS) platform. The AbsoluteIDQ® p 180 Kit (Biocrates Life Sciences AG, Innsbruck, Austria) was used for metabolite profiling, and the sample preparation methodology recommended by the manufacturer was followed. 96-well plates (total of 23 well plates) were used to prepare samples, and matching case-control sets were measured on the same plate. The case-control status of the samples was hidden from laboratory employees. Even after controlling for BMI and other endometrial cancer risk factors, glycine, serine, and free carnitine levels were inversely, and the sphingolipidSM C18:0 favourably, linked with endometrial cancer risk in this large-scale prospective analysis of endometrial cancer. Furthermore, the ratio of esterified to free carnitine, as well as the ratio of short chain acylcarnitines to free carnitine, were also found to be positively linked with the risk of endometrial cancer. After controlling for multiple comparisons, none of these correlations remained statistically significant. Only a few researches have looked at metabolite profiles in relation to endometrial cancer risk, and they were all tiny sample studies. Cancer Research UK (CRUK) funded this research (grant number C19335/A21351, to MJG and HK). The Imperial College Experimental Cancer Medicine Centre, the Imperial College Cancer Research UK Centre, and the NIHR Imperial Biomedical Research Centre all support the metabolomics infrastructure at the Division of Cancer at Imperial College London (APS & HK). The International Agency for Research on Cancer (IARC) and the Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, which has additional infrastructure support supplied by the NIHR Imperial Biomedical Research Centre, are funding EPIC's coordination (BRC). Mean and standard deviation (SD) or frequencies were used to represent case and control characteristics. All analyses used log-transformed metabolite concentrations. The risk of endometrial cancer was calculated using conditional logistic regression for each standard deviation (SD) rise in log metabolite concentration. We also looked into the relationship between endometrial cancer risk and particular metabolic ratios and sums. Body mass index (BMI) and waist circumference were also factored into the models. EPIC is a multi-centre cohort study with around 520,000 participants recruited from ten European nations in the early 1990s. At the time of recruitment, complete information on nutritional, lifestyle, reproductive, medical, and anthropometric data was gathered, as well as a baseline blood sample from the majority of individuals. To take part in the EPIC trial, all participants signed a written informed permission form. The International Agency for Research on Cancer (IARC) ethical committee and all centres authorised this study.

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