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Circulating plasma phospholipid fatty acid levels and breast cancer risk in the CPS-II Nutrition Cohort

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Background
The association between dietary fat intake and breast cancer risk has been a source of controversy with conflicting results reported in past decades. Additional prospective studies that objectively measure circulating levels of fatty acids are now needed to better understand the associations between dietary fat and breast cancer development.

Methods
We assessed the relation between breast cancer risk and plasma levels of 60 phospholipid fatty acids in a nested case-control study of 2,718 postmenopausal women (905 breast cancer cases and 1,813 matched controls) enrolled in the Cancer Prevention Study II (CPS-II) Nutrition Cohort. Blood samples were collected at baseline (1997-1998). Multivariable-adjusted conditional logistic regression models that included established breast cancer risk factors (alcohol use, postmenopausal hormone use, smoking status, waist circumference, body mass index, and weight change from age 18 years to blood draw) were used to compute odds ratios (OR) and 95% confidence intervals (CI). The false discovery rate (FDR; q-value) was computed to control for multiple comparisons.

Results
After adjustment for multiple comparisons and in continuous log-transformed multivariable models, plasma levels of myristic acid (a saturated fatty acid) were positively associated with breast cancer risk (OR per log-value, 1.17, 95% CI: 1.07-1.28; q-value = 0.03), with similar magnitude associations found for estrogen receptor (ER) positive and ER negative breast cancer (p-interaction = 0.39). Positive associations were also found for plasma levels of monounsaturated fatty acid (OR per log-value, 1.09, 95% CI: 1.00-1.18; q-value = 0.24), palmitoleic acid (OR per log-value, 1.14, 95% CI: 1.04-1.24; q-value = 0.09), palmitic acid (OR per log-value, 1.12, 95% CI: 1.01-1.24; q-value = 0.17), dihomo-γ-linolenic acid (OR per log-value, 1.14, 95% CI: 1.04-1.25; q-value = 0.09), and adrenic acid (OR per log-value, 1.13, 95% CI: 1.03-1.24; q-value = 0.11) with breast cancer risk; however, after adjustment for multiple comparisons these associations did not reach the threshold of statistical significance. Similarly, inverse associations between plasma levels of trans α-linolenic acid (OR per log-value, 0.85, 95% CI: 0.76-0.96; q-value = 0.09), heptadecanoic acid (OR per log-value, 0.90, 95% CI: 0.82-0.99; q-value = 0.17), and vaccenic acid (OR per log-value, 0.88, 95% CI: 0.80-0.97; q-value = 0.11) with breast cancer risk were not statistically significant after adjustment for multiple comparisons.

Conclusion
These findings suggest that higher circulating levels of myristic acid, that can be sourced from dietary intake of dairy foods or via de novo synthesis, may increase breast cancer risk. Additional studies are needed to replicate this finding and provide mechanistic insights.

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