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The impact of dietary saturated fat replacement with unsaturated fat on the plasma lipidome and cardiometabolic disease risk

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Evidence from epidemiological studies and randomised controlled trials (RCTs) suggests that replacing dietary saturated (SFAs) with unsaturated fatty acids (UFA) may have beneficial impacts on cardiometabolic disease (CMD) risk[(1)]. However, interdisciplinary research narrowing the gap between interventional and observational evidence is lacking. Recent findings have suggested the utility of high-throughput lipidomics to identify potential CMD risk markers and provide novel aetiological insights into the relationship between dietary fat composition and CMD risk[(2)]. Thus, this study aimed to assess the lipidome-mediated impact of replacing dietary SFAs with UFAs on CMD risk.

Plasma fatty acid (FA) concentrations among 14 lipid classes were measured using high-throughput lipidomics analyses (Metabolon, USA) in samples from the DIVAS parallel RCT (n = 113), which investigated the effects of three 16-week diets enriched in SFAs (target SFA:monounsaturated fatty acids MUFA:*n-6* polyunsaturated fatty acids PUFA ratio = 17:11:4% total energy TE), MUFAs (target SFA:MUFA:*n-6*PUFA ratio = 9:19:4%TE), or a mixture of UFAs (target SFA:MUFA:*n-6*PUFA ratio = 9:13:10% TE) on CMD risk markers such as fasting lipid profiles, and markers of inflammation, endothelial function, and arterial stiffness[(3)]. Similar lipidomics analyses were conducted on samples from two case-cohorts from the EPIC-Potsdam prospective cohort study [n = 1,707 for type 2 diabetes (T2D) and n = 1,886 for cardiovascular diseases (CVD)][(2)]. Within-class FAs sensitive to the DIVAS dietary intervention were identified using multiple linear regression models and related to CMD risks in each EPIC-Potsdam case-cohort using multivariable Cox proportional hazard models. Finally, within- class FAs associated with changes in CMD risk markers assessed in the DIVAS study were identified using constraint-based feature selection algorithms and multiple linear regression models.

Analysis of within-class plasma FA concentrations revealed high-UFA intervention diets from the DIVAS study broadly reduced the concentrations of FAs associated with higher CVD risk, and to a lesser extent T2D risk, in the EPIC-Potsdam cohort, such as palmitic (16:0) and stearic (18:0) acids in di- and triacylglycerol, and myristic acid (14:0) in hexosylceramides, with clearer effects of the high- MUFA diet compared to the mixed-UFA. Reciprocally, the high-UFA diets increased the concentrations of FAs associated with lower CMD risk, such as erucic acid (22:1) in triacylglycerol and nervonic acid (24:1) in lactosylceramides. Furthermore, increased low-density lipoprotein cholesterol and total cholesterol concentrations were associated with a higher abundance of arachidic acid (20:0) in cholesteryl esters and diacylglycerol ($p < 10^{-3}$ and $p = 0.001$, respectively), whilst increased interleukin-6 and P-selectin concentrations were associated with higher proportions of arachidic acid (20:0) in mono- ($p = 0.008$) and triacylglycerol ($p = 0.02$).

Overall, these findings suggest a potential mediating role of plasma lipid metabolites in the association between dietary fat and CMD risk. Future research combining interventional and observational findings and investigating the identified within-class FAs is warranted to improve our understanding of dietary fat composition in CMD aetiology.

References

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