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## Associations between dietary fatty acids and liver fat accumulation in the UK Biobank

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Steatotic liver disease, defined as >5% of hepatic fat content, is a major contributor to global morbidity and mortality, in particular due to its category metabolic associated steatotic liver disease (MASLD)<sup>(1)</sup>. While its prevention focuses on promoting physical activity and maintaining a healthy weight and balanced diet, the associations between dietary fatty acids and liver fat remain unclear<sup>(2,3)</sup>. The aim of this study was to examine the associations between dietary fatty acids and liver fat in the absence of excessive alcohol intake, independently of energy intake.

Analyses were conducted on 9,268 non-diabetic participants from the UK Biobank with no pre- existing liver chronic illness or cardiovascular disease at baseline, and without excessive alcohol consumption. Dietary intake of total fat, saturated fatty acids (SFAs), polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) was measured using the mean of  $\geq 2$  Oxford WebQ 24-hr dietary assessments, responded to between 2009 and 2012. Liver proton density fat fraction (LPDFF) was measured by magnetic resonance imaging between 2016 and 2020. Multivariable linear regression models were calculated to assess the associations between fatty acid intakes and LPDFF, adjusting for key demographic and lifestyle confounders. In addition, associations between LPDFF and 10 individual SFAs, 7 PUFAs, and 4 MUFAs were also examined. Sensitivity analyses were carried out including participants who responded  $\geq 4$  dietary assessments (N=2,828).

After fully adjusting for confounders, no significant associations between LPDFF (%) and MUFAs were found. Inverse associations with LPDFF were observed for PUFAs (-5.8% relative difference [95% confidence interval -0.6, -1.9]), per 5% increase in intake, while SFAs were positively associated with LPDFF (5.8% [3.3, 8.3]). Positive associations were observed per 1 SD increase in intake of individual fatty acids SFA stearic acid (4.20% [2.84, 5.57]) and palmitic acid (3.15% [1.78, 4.54]). Negative associations were observed for PUFAs alpha-linoleic acid (-2.32% [-3.47, -1.17]) and docosahexaenoic acid (-2.14% [-3.23, -1.0.3], and for MUFA erucic acid (-2.52% [-3.61, -1.43]). Sensitivity analyses presented similar results, and the associations between PUFAs and liver fat became slightly stronger (-10.73%, [-17.58, -3.32]).

This observational study suggests that SFAs and PUFAs are associated with liver fat in opposite directions, independently of energy intake. While total MUFAs did not present significant associations with LPDFF, erucic acid was inversely associated with liver fat, highlighting the value of studying individual fatty acids. These different associations provide valuable information for the design of dietary trials that compare interventions with different types of fatty acids. These further studies would allow a better understanding of the ideal dietary advice to prevent liver steatosis and its global health impact.

## References

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