Uncovering the shared lipidome-wide markers of carotid artery atherosclerotic plaque and metabolic associated fatty liver disease (MAFLD) in non-overlapping Individuals: The Young Finns study

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Background: Metabolic associated fatty liver disease (MAFLD) and carotid artery atherosclerotic plaque diseases are both linked to circulatory lipid and lipoprotein metabolism. However, shared lipidomic-wide mechanisms underlying these diseases in non-overlapping populations remain unexplored.

Objectives: To identify plasma lipid species associated with both MAFLD and carotid artery plaque diseases in order to uncover shared metabolic pathways.

Subjects and Methods: We analyzed data from the Young Finns Study cohort from 2007 and 2018 follow-ups (n=1496, aged 41-56 years, 56.3% females). Ultrasound was used to determine the prevalence of both carotid atherosclerosis plaques and MAFLD during 2018 follow-up. Participants were divided into two subsets of not overlapping subjects: 693 with only carotid plaque but without MAFLD and 586 with only MAFLD but without carotid plaque. Lipidomic profiling of 437 lipid species from plasma was performed during 2007 follow-up (30-45 yrs) using liquid-chromatography-tandem mass spectrometry. Logistic regression models, unadjusted and adjusted for age, sex, physical activity, alcohol consumption, and smoking, were used to separately assess lipid associations with both disease outcomes. Odds ratios (OR) and confidence intervals (95% CI) were calculated for each lipid species, and multiple testing corrections were performed using the false discovery rate (FDR) method (< 0.05).

Results: In unadjusted and adjusted models, 80 and 4 lipids respectively, were significantly associated with carotid plaque. In adjusted model, 202 lipids were linked to MAFLD. In unadjusted model, we

found 51 lipids significantly associated with both diseases. Notably, in the adjusted models only one lipid, PC 40:4, was significantly associated with both diseases, and significantly increased risk of disease in both conditions OR 2.59 (95% CI, 1.57- 4.32) and OR 5.26 (95% CI, 2.81- 9.85) for carotid plaques and MAFLD, respectively.

Conclusion: Our findings identify PC 40:4 as a shared lipid signature between MAFLD and carotid plaque disease, suggesting common metabolic pathways.

Keywords: Lipidomics, cardiovascular disease, fatty liver, carotid plaque, phosphatidylcholine