Ceramides are related to subclinical atherogenesis in the general population

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Introduction: Biomarkers for risk stratification of patients with cardiovascular disease are essential for disease prevention. Ceramides play an important role during atherogenesis. For the C24:0/C16:0 ratio an inverse association with incident coronary artery disease and heart failure has been shown. Hence, ceramides may be a new predictive biomarker for cardiovascular disease.

Purpose: We explored the relation of three specific ceramides (i.e. C16:0, C22:0 and C24:0) and their ratios with subclinical atherosclerosis, assessed by carotid intima media thickness (cIMT), carotid lumen diameter (LD), brachial artery flow mediated dilation (FMD), nitroglyceride mediated brachial artery dilation (NMD) as well as with the presence of atherosclerotic plaques in the common carotid artery, the carotid bifurcation, and the internal as well as external carotid artery.

Methods: We used data from the population-based Study of Health in Pomerania (SHIP-1) from North-East Germany (n=2,506, 47% male, 53 median age, 25th and 75th inter-quartile range 41–64 years). Ceramides were quantified by liquid chromatography/tandem mass spectrometry assay. Extracranial carotid arteries were measured with B-mode ultrasound and used to assess plaque presence, LD, NMD, FMD and cIMT with standard procedures. Subjects with missing data were excluded. The relationship between ceramides and log LD, log cIMT, NMD, FMD as well as plaque score were modelled using multivariable regression models adjusted for sex, age, body mass index, diabetes mellitus, dyslipidaemia, hypertension and smoking status.

Results: A 1 μg/ml higher C22:0 and C24:0 were associated with a 3% (95% confidence interval [CI] 1% - 5%, $p<0.01$) and 1% (95% CI 0% - 1%, $p=0.01$) smaller LD, respectively. Furthermore, an increased C22:0/C16:0 and C24:0/C16:0 ratio were related to a 1.2% (95% CI 0.6% - 1.8%) and 0.2% (95% CI 0.009% - 0.37%, $p<0.01$) narrower LD, respectively. A one point higher C22:0/C16:0 ratio was associated with a 0.04 mm (95% CI 0 – 0.08 mm, $p=0.04$) greater absolute FMD. Moreover, a 1 μg/ml higher C16:0 or C22:0 concentration increased the odds for the presence of plaque by 13.6% (95% CI 2.33–79.0, $p<0.01$) and 1.68% (95% CI 1.08–2.61, $p=0.02$). Neither C24:0 nor the C22:0/C16:0 or C24:0/C16:0 ratios were related to the presence of atherosclerotic plaques and did not find any significant associations between ceramides and cIMT or NDM.

Conclusions: We found significant associations of ceramides with various markers of subclinical atherosclerosis. Hence, our findings further support the investigation of ceramides as biomarkers of vascular disease. However, our results indicate that not all ceramides are equal with regards to atherosclerosis. For example, C22:0 is related with vasoprotective effects (high HDL-C, low triglycerides) and intriguingly, more atherosclerotic plaques. Future studies should explore the role of ceramides during the different stages of atherosclerosis.