The functional relevance of HDL structure and composition in the improvement of cholesterol efflux capacity after Roux-en-Y gastric bypass

Authors:
A Jomard⁠¹, P Doytcheva², J Deuel³, T Luscher², C Wolfrem¹, T Lutz², E Osto², ¹Swiss Federal Institute of Technology Zurich (ETH Zurich), Laboratory of Translational Nutrition Biology - Zurich - Switzerland, ²University of Zurich, Center for Molecular Cardiology - Zurich - Switzerland, ³University Hospital Zurich, Internal medicine - Zurich - Switzerland,

Topic(s):
Lipids, Metabolism

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S130

Funding Acknowledgements:
SNSF Ambizione Grant (PZOOP3_161S0S /1 to EO); the Swiss Card-Onco-Grant - Alfred and Annemarie von Sick Grant, Swiss Lipid Research Award 2016 to EO.

Background: Roux-en-Y gastric bypass (RYGB) reduces cardiovascular mortality. We showed that RYGB improves HDL cholesterol efflux capacity. The structure and molecular composition may be a crucial determinant of HDL functionality. Purpose: We studied whether and how changes in HDL subclasses profile and phospholipid (PL) composition after RYGB correlate with HDL cholesterol efflux capacity.

Methods: HDL subclasses profile was assessed by fast protein liquid chromatography (FPLC) and by NMR from 15 morbidly obese patients before and 1 year after RYGB. After FPLC, cholesterol efflux was measured in J774 macrophages stimulated with HDL large, medium and small. Furthermore, the PL composition of different HDL subclasses was quantified by liquid chromatography-mass spectrometry (LC/MS).

Results: FPLC showed increased smaller size HDL 1 year after RYGB (small HDL-1Y) compared to baseline. The size-function analysis revealed that among all HDL subclasses, small HDL-1Y were the most potent stimulator of cholesterol efflux from J774 macrophages. NMR analyses revealed also higher HDL particles number. Further, the composition of the small HDL-1Y showed specific elevation of certain phosphatidylethanolamines (PC), phosphatidylserine (PS) and phosphatidic acid (PA) content, as well as some corresponding lyso-forms (PA, PC, PE) compared to small HDL of the same patients before RYGB. Enrichment of HDL with these specific PL is correlated to an enhanced cholesterol efflux capacity and may underline the improved HDL functionality after RYGB. Reduced sphingosine-1-phosphate (S1P) content is a known mediator of HDL dysfunction. Indeed, S1P content was also increased in small HDL-1Y after RYGB. Total HDL cholesterol concentration was increased post RYGB.

Conclusions: Small HDL-1Y after RYGB are increased and have enhanced cholesterol efflux capacity. Elevated content in PC, PS, PA and their lyso-forms as well as increased S1P levels may contribute to the improved athero-protective function of small HDL-1Y after RYGB. RYGB seems to achieve a dual benefit increasing the concentration and function of HDL.