EAS-0517.
MODIFICATION OF LIPOPROTEIN AND GLUCOSE METABOLISM, VASCULAR INFLAMMATORY BIOMARKERS AND NEUROPATHY AFTER WEIGHT LOSS FOLLOWING BARIATRIC SURGERY

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Aim: To investigate the impact of weight loss following bariatric surgery on lipoproteins, glucose metabolism, vascular inflammatory markers and neuropathy.

Methods: 27 obese patients (11 with type 2 diabetes) and 28 healthy controls were recruited. Lipid, glycaemic and vascular biomarkers were measured before, and 6 and 12 months after bariatric surgery. The effect of weight loss on neuropathy was assessed in a subgroup of 10 patients before and 6 months after surgery.
Results: After surgery glycated apolipoprotein B ($p<0.0001$), body mass index, waist circumference, glycated haemoglobin, fasting glucose, insulin, Homeostasis Model Assessment (HOMA)-B, HOMA-IR, small-dense low-density lipoprotein (LDL), high-sensitivity C-reactive protein, E-selectin, intercellular adhesion molecule (all $p=0.0001$), triglycerides ($p=0.0002$), monocyte chemotactic protein-1, apolipoprotein A-II (both $p=0.0004$), tumour necrosis factor-a ($p=0.0006$), resistin ($p=0.0009$), acylation stimulating protein ($p=0.001$), cholesteryl ester transfer protein activity ($p=0.0018$), interleukin-6 ($p=0.002$), cholesterol, apolipoprotein B, leptin (all $p=0.01$), P-selectin ($p=0.018$), LDL and blood pressure (both $p=0.03$) decreased significantly. Bioimpedance, adiponectin (both $p=0.0001$), high-density lipoprotein (HDL) ($p=0.002$) vascular cell adhesion molecule ($p=0.0035$), paraoxonase-1 ($p=0.005$) and oxidised-LDL ($p=0.0062$) were significantly increased. We also for the first time report the effect of weight loss following bariatric surgery on proprotein convertase subtilisin/kexin type 9, apolipoprotein M, malondialdehyde, myeloperoxidase, oxidised-HDL and cholesterol efflux capacity, and associated improvements in markers of small fibre neuropathy.
Conclusions: Lipoproteins, glucose metabolism and vascular inflammatory biomarkers improved with weight loss following surgery. Our results suggest that the presence of diabetes is associated with a delay in improvements of some biomarkers associated with cardiovascular risk after bariatric surgery.

EAS-0615.
FATTY ACIDS COMPOSITIONS AND CEREBRAL SMALL VESSEL DISEASE

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Background: Cerebral small vessel diseases (SVDs) are related with stroke or cognitive dysfunction. Meanwhile, ω3-polyunsaturated fatty acids (FAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are highlighted as disease modifying factors for cardiovascular disease.

Objectives: In this study, the association between composition of plasma FAs and cerebral SVDs were investigated in ischemic stroke patients.
Methods: We prospectively enrolled 220 patients with first-episode cerebral infarction within 7 days after symptom onset. The composition of FAs was analyzed by gas chromatography methods. The presence of cerebral microbleeds (CMBs), high grade white matter changes (HWCs) by Fazekas' grading system and asymptomatic lacunar infarctions (ALIs) were investigated.
Results: The mean proportion of EPA was 2.0 ± 0.7, DHA was 8.9 ± 1.5 and that of ∑ ω3-polyunsaturated fatty acids (PUFAs) was 12.0 ± 2.1. In total patients, 46 (20.9%) patients had CMBs, 64 (29.1 %) had HWCs and 65 (29.5%) had ALIs. The proportion of ω3-PUFAs was associated with presence of CMBs but not independently. Considering HWCs, lower proportion of EPA, DHA and ∑ ω3-PUFAs were independent predictors for presence of HWCs (odds ratio (OR): 0.44, 0.72 and 0.74, respectively). Moreover, lower proportion of ∑ ω3-PUFA was determinant factor for existence of ALIs (OR: 0.84).
Conclusions: Our results demonstrate ω3-PUFAs are associated with cerebral SVDs in acute stroke patients. The ω3-PUFAs are potential biomarkers for predicting SVDs in stroke.

EAS-0688.
THE ROLE OF E2F1 IN CHOLESTEROL METABOLISM

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Cholesterol is a sterol molecule required for the synthesis of cell membrane and many steroid hormones. Physiologically, cholesterol level is rigorously regulated and deviation is associated with clinical consequences. Previous lab data from chip-seq has revealed that several E2F1 target genes were implicated in cholesterol metabolism pathway. Interestingly, E2F1-/- mice were shown to display lower plasma cholesterol level as compared to wild type mice. To further elucidate the interaction between E2F1 and cholesterol metabolism, we studied the activities of cholesterol related genes in *in vivo* and *in vitro* system. Our data suggested that E2F1 is necessary to regulate cholesterol homeostasis. In E2F1-/- hepatocytes, we found a reduction in the rate of cholesterol biosynthesis, which indicates that E2F1 plays a role in regulating biosynthesis pathway. Consistently, cholesterol synthesis genes such as HMGCR, HMGCR and SREBP2 were decreased in E2F1-/- hepatocytes. Additionally, we also found that increasing E2F1 transfection enhanced SREBP2 promoter activity, suggesting that E2F1 is necessary for SREBP2 activation. Further studies aim to describe the biological mechanism of E2F1 regulating cholesterol biosynthesis and characterize the function of E2F1 in atherosclerosis mouse model.

Emerging aspects in pharmacological treatment of primary and secondary dyslipidemia

EAS-0040.
ACUTE AND PROLONGED CHANGES IN LIPOPROTEIN PROFILE IN HUMAN VOLUNTEERS TREATED WITH SINGLE ASCENDING DOSES OF MDCO-216 (APOA1-MILANO/POPC)

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We studied the effects of single ascending doses of MDCO-216 on lipid and (apo)lipoprotein levels and particle sizes measured by 2D electrophoresis, NMR and FPLC in human volunteers. Doses of 5, 10, 20, 30 and 40 mg/kg were infused over 2 h and plasma and serum were collected over 30 days. 2D gel electrophoresis showed: (i) increases in prebeta-1 HDL (up to 3-fold above baseline) and alpha-2 and alpha-1 HDL and drop of alpha-4 and alpha-3 HDL immediately after infusion and at all doses; (ii) apoA-IM was detected in alpha-2 and alpha-1 HDL at all doses and time points but was never detected in prebeta-1 HDL. NMR analysis likewise showed a rapid and dose-dependent shift from small-sized to larger-sized HDL particles at all doses. LDL and VLDL-particles also increased in size, but only at the highest doses. FPLC analysis for the 40 mg/kg dose showed an initial rise in HDL-free cholesterol (FC) returning to baseline at 24 h followed by an increase in non-HDL-FC still observed at day 7. HDL-CE initially increased but after 24 h decreased below baseline; non-HDL-CE increased and was still above baseline at day 7. Plasma cholesterol esterification rate was decreased at 4-8 h but returned to baseline thereafter. We conclude that MDCO-216 rapidly fuses with small HDL to produce larger HDL displacing