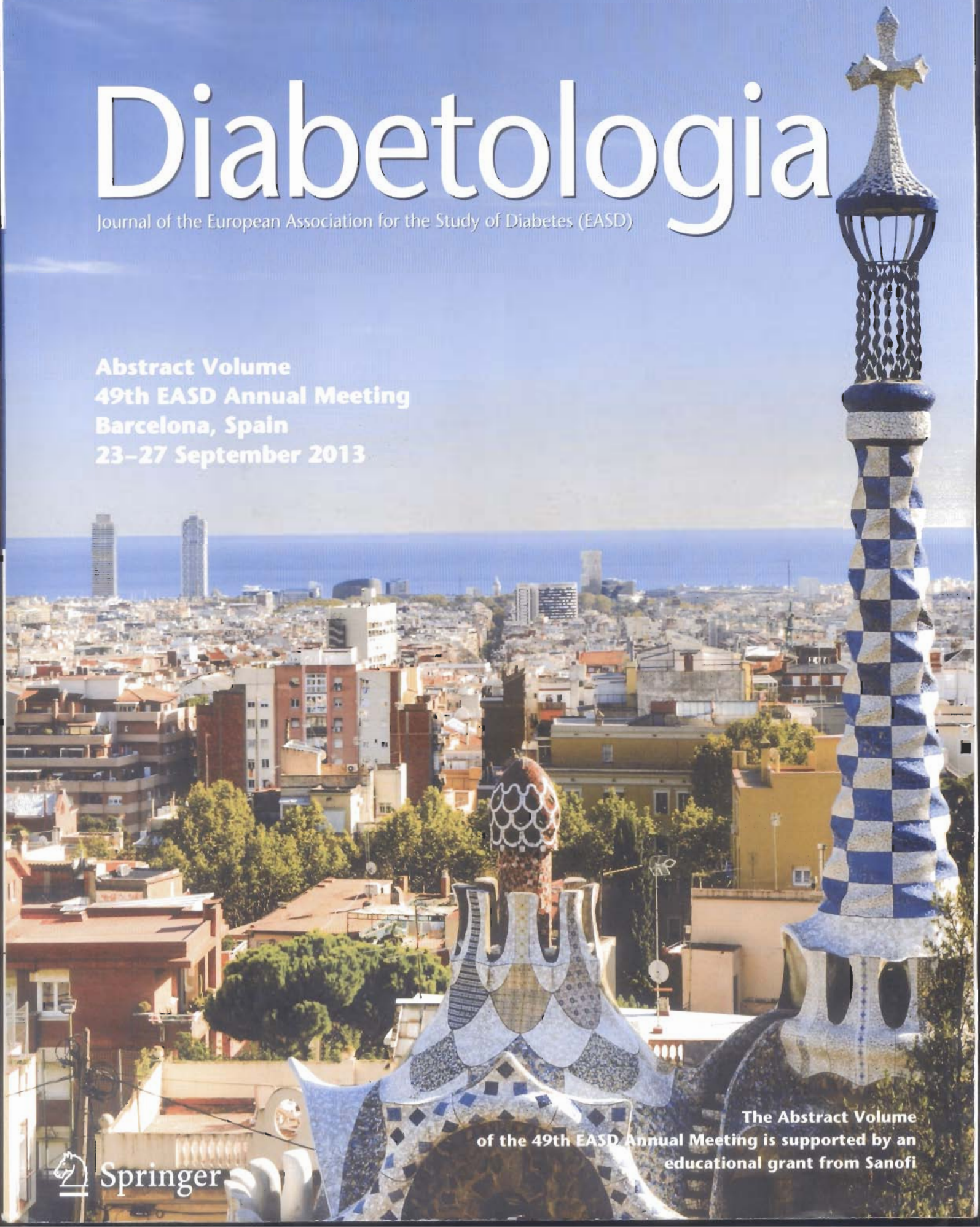
Volume 56 | Supplement 1 | 2013

Diabetologia

Journal of the European Association for the Study of Diabetes (EASD)

Abstract Volume
49th EASD Annual Meeting
Barcelona, Spain
23–27 September 2013



The Abstract Volume of the 49th EASD Annual Meeting is supported by an educational grant from Sanofi

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(γ=-0.164,P<0.01) after adjustment for gender, age, BMI, and oral anti-diabetic drugs. Meanwhile, duration of diabetes was also correlated with NFS positively (γ=0.236,P<0.01). Multiple linear regression analysis showed that the liver fat content was independently associated with duration of diabetes.
Conclusion: With the extension of the duration of diabetes, the reduction of liver fat content of type 2 diabetic patients with NAFLD is related to the development of advanced fibrosis. Decline in liver fat content of type 2 diabetic patient is associated with poor outcome of non-alcoholic fatty liver disease.

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The change in plasma triglycerides during an OGTT strongly predicts nonalcoholic fatty liver disease and the effectiveness of a lifestyle intervention to reduce liver fat

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Background and aims: It was recently shown that the change of plasma triglyceride levels during a standard oral glucose tolerance test (OGTT) is associated with visceral fat and insulin resistance. We therefore hypothesized that it may also be a predictor of nonalcoholic fatty liver disease (NAFLD) and may be associated with the change of liver fat content during a lifestyle intervention in humans.
Materials and methods: In 330 individuals at risk of type 2 diabetes, liver fat content was quantified by ^{1}H-magnetic resonance spectroscopy. Liver enzymes, lipids and lipoprotein levels were measured during fasting and after a 2hr-75g OGTT. A subgroup of 213 individuals underwent these measurements before and after participating for 9 months in the Tübingen Lifestyle Intervention Program (TULIP).
Results: In all subjects at baseline, the change in plasma triglycerides during the OGTT (120min-0min; ΔTG_{OGTT}) more strongly associated with liver fat content (r=0.51; r=0.28 after adjustment for gender, age, total body- and visceral fat), and more accurately predicted NAFLD (ROC-AUC=0.75 and 0.83) than fasting liver enzymes, lipids and lipoproteins and 2h-triglycerides (all r<0.49 and ROC-AUCs<0.82). During the lifestyle intervention, ΔTG_{OGTT} at baseline strongly predicted (adjusted estimate±SE: 1.04±0.29) change of liver fat content (estimates for all other parameters <0.24±0.08). After correction for confounders, the odds ratio for 1 standard deviation decrease in TG_{OGTT} at baseline for subjects to experience a reduction in liver fat content during the intervention was 1.90 (95% confidence interval, 1.25-2.97).
Conclusion: We provide novel data that, among commonly measured blood parameters, ΔTG_{OGTT} strongly and independently predicts NAFLD. Moreover, ΔTG_{OGTT} may become an interesting parameter being able to predict the change of liver fat content during a lifestyle intervention in subjects who are at risk for type 2 diabetes.

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Alteration in lipid metabolism after an oral fat load in subjects with NAFLD

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Background and aims: Subjects with non alcoholic fatty liver disease (NAFLD) are at high risk to develop type 2 diabetes and cardiovascular diseases. Hepatic fat accumulation (IHTG) is the results of insulin resistance (IR) and the impairment in hepatic lipid metabolism. Hepatic TG accumulate because after synthesis they cannot be exported as VLDL or oxidized. In subjects with NAFLD VLDL secretion is often increased as well as hepatic fat oxidation, so probably these two processes are saturated determining IHTG. Thus, we have studied the effect of a lipid load on peripheral lipolysis and hepatic lipid metabolism.
Materials and methods: We have studied glucose and lipid metabolism after a lipid load (200ml dairy cream and egg yolk) in 21 subjects, 15 with biopsy proven NAFLD and 6 controls, CT (mean age 35, BMI 25 kg/m2). Tracers (6,6-2H2-glucose and 2H5-glycerol) were infused for 120min before meal, and 240min after lipid load to evaluate glucose metabolism (EGP and clearance) and lipolysis. Throughout the test we measured glucose, insulin, FFA, triglyceride, cholesterol profiles. During fasting Peripheral IR was measured as HOMA (peripheral), hepatic IR as Hep_IR=EGPxINS, adipose IR as Adipo_IR=lipolysisxINS)
Results: Subjects with NAFLD had higher LFTs (ALT 68±8 vs 16±2 U/l, AST 34±3 vs 19±2 U/l, GGT 92±20 vs 15±6 U/l, all p<0.03), triglycerides (TG 121±12 vs 45±5 p<0.01), insulin (INS 11±2 vs 6±1 p<0.01) but similar fasting plasma concentrations of glucose (98±3 vs 90±2 mg/dl), FFA (0.57±0.08 vs 0.61±0.06 mmol/l), total cholesterol (198±8 vs 163±13 mg/dl), HDL cholesterol (49±2 vs 54±11 mg/dl), ApoB (90±8 vs 64±9 mg/dl). During fasting EGP was similar in both groups (8.8±0.4 vs 8.2±0.4 umol/kg min) while lipolysis was increased in subjects with NAFLD (2.2±0.2 vs 1.5±0.1 umol/kg min p=0.05) that were also more insulin resistant than CT (HOMA 2.8±0.5 vs 1.3±0.2, Hep_IR 101±18 vs 45±6, Adipo_IR 25±5 vs 9±2 all p<0.01). After the oral lipid load insulin increased slightly and as a consequence EGP and glucose concentrations did not change from baseline in CT and slightly decreased in NAFLD (from 8.8±0.4 at t=0 vs 7.8±0.4 umol/kg min at t=240, p<0.05). On the other hand lipolysis did not change in NAFLD, while it was significantly suppressed at 30 min in CT (to 0.9±0.1 umol/kg min p=0.02) to return to baseline at 240min. Cholesterol profile did not change while FFA concentrations increased similarly in the two groups. On the other hand TG increase after lipid load was more pronounced in NAFLD vs CT, AUC-TG increased by 50% (p<0.02) and iAUC-TG was increased 2 folds (p<0.03), reaching a maximum at 4h.
Conclusion: The metabolic handling of an oral fat load is impaired in subjects with NAFLD: basal increased lipolysis was not suppressed after a lipid load, as occurred in CT, and postprandial triglyceride increase was more pronounced. All these alterations might contribute to the development and progression of fatty liver disease.
Supported by: FLIP- FP7 project, HEALTH-F2-2009-241762

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Interaction between obesity status and dietary intakes of sucrose and ω-6/ω-3-polyunsaturated fats and the Ile148Met in the PNPLA3 gene

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Background and aims: The Ile148Met (rs738409) in the patatin-like phospholipase domain-containing protein 3 gene (PNPLA3) associates with non-alcoholic fatty liver disease (NAFLD) and the PNPLA3-148M (G-allele) has been suggested to lead to both loss-of-function (hydrolysis) and gain-of-function [CoA- dependent lysophosphatidic acid acyltransferase (LPAAT)] defects. PNPLA3 is up-regulated by dietary carbohydrates (CHO), it has a higher affinity for unsaturated fatty acids and interactions between rs738409 and dietary intakes of CHO, sucrose and ω-6/ω-3-polyunsaturated fats (ω-6/ω-3-PUFA) on hepatic fat accumulation have been reported. We examined the interaction between rs738409 and obesity status on fasting triglyceride and alanine aminotransferase (ALT) levels, and the interaction between rs738409 and intakes of CHO, sucrose and ω-6/ω-3-PUFA on fasting triglyceride levels.
Materials and methods: From the Malmo Diet and Cancer Cardiovascular Cohort (MDC-CC) 4827 non-diabetic individuals aged 58±6.0y, 3343 with BMI≤27kg/m2 and 1481 with BMI>27kg/m2 were included in analyses. Dietary data was collected by a modified diet history method.
Results: Obesity status modified the association between rs738409 and fasting triglyceride- and ALT-levels (Pinteraction=0.006 and 0.01). The NAFLD-risk G-allele associated with lower triglyceride and higher ALT levels only among overweight individuals (P=0.005, P=0.0002). Significant interactions on triglyceride levels were observed between rs738409 and sucrose among normal weight individuals (Pinteraction=0.02) and ω-6/ω-3-PUFAs among overweight individuals (Pinteraction=0.03). G-allele associated with lower triglycerides only among overweight individuals in the lowest intake tertiles of CHO, sucrose and ω-6/ ω-3-PUFAs (P=0.007, P=0.03, P=0.0004) and with higher triglycerides only among normal weight individuals in the highest intake tertile of sucrose (P=0.02).
Conclusion: Obesity status and dietary sucrose and ω-6/ω-3-PUFA intakes modify the association between rs738409 and fasting triglyceride levels. Our