Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world; its prevalence has increased recently, accompanied by global obesity pandemic. It is a complex entity that arises from numerous genetic, environmental, behavioral and social factors. Non-alcoholic steatohepatitis (NASH) is part of the disease progression and is a preamble to more severe complications such as cirrhosis and hepatocellular carcinoma. Currently, the only tool to diagnose NASH is liver biopsy. The aim is to identify the different microRNAs (miRNAs) involved in NAFLD progression.

Method: 117 patients were recruited; liver biopsy and a blood sample were obtained; 30 were submitted to microarray assays and classified according to controlled attenuation parameter (CAP) and NAFLD activity score (NAS). Patients with CAP ≤232 dB/m, 0-point NAS and histopathological report without alterations, were the control group; with CAP ≥290 dB/m, NAS ≥1 to 3 points and histopathological report with steatosis in more than 5% of hepatocytes, were the NAFLD group; and patients with CAP ≥290 dB/m, NAS ≥5 points and histopathological report with steatosis accompanied by inflammatory ballooning and fibrosis, were the NASH group. From blood samples, liver function tests, as well as fasting cholesterol, triglycerides, and glucose levels, were determined. RNA was extracted from liver tissue to analyze the miRNAs differential expression using the GeneChip miRNA 4.0 microarray; expression levels were compared with the Affymetrix TAC software using a fold change parameter ≥2 and ≤−2; FDR ≤0.05 and p ≤0.001.

Results: Regarding the anthropometric characteristics, BMI had a statistical difference between control 27.8 kg/m², NAFLD 29.1 kg/m² and NASH 39.1 kg/m² p < 0.0001; liver function profile, circulating lipids and fasting glucose did not change. The miRNA expression reveals a differential expression of 24 miRNAs in the NAFLD group, 23 were upregulated and 1 downregulated; miR-122-3p was expressed 9 times more than the control, followed by the miR-140-5p that showed almost 6 times more expression, the miR-200a-3p was 5 times more expressed, but also the miR-148a-3p and the miR-148a-5p were 4 times more expressed than the control; while the miR-6089-2 shows 2-fold drop expression compared to the control group. While NASH results disclosed 21 differentially expressed miRNAs compared to controls, miR-297, miR-3064-5p, miR3148 and miR-7844-5p showed more than 2 times decrease expression compared to the control group.

Conclusion: The results suggest that miRNAs differential expression could be used as potential NAFLD diagnostic and progression biomarkers; however, the mechanism by which these miRNAs are involved in the pathogenesis needs further investigation.

SAT022
Simultaneous intra-operative sampling from multiple anatomical sites reveals pro-inflammatory liver homing T cells in liver, adipose tissue and peripheral blood in patients with NASH
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Background and Aims: Non-alcoholic steatohepatitis (NASH) is an inflammatory liver disease that can lead to fibrosis, cirrhosis and end stage liver disease. NASH has a multi-directional relationship with metabolic syndrome. Emerging evidence suggests an increase in peripheral blood Th1 helper 1 (Th1) cells in NASH. However, the number and phenotype of T cells sampled simultaneously from adipose and liver tissue and peripheral blood in obese patients with NASH has not been studied to date. Here we test the hypothesis that a Th1 phenotype is dominant in all anatomical compartments.

Method: Patients undergoing bariatric surgery with NAFLD underwent simultaneous sampling of liver, visceral and subcutaneous adipose tissue and peripheral blood mononuclear cells for immunoprofiling by flow cytometry.

Results: We included 15 bariatric patients (median age 54); 6 with biopsy-proven NASH and 9 non-NASH. NASH patients had greater median BMI 49.8 (IQR 48.1–52.9) than non-NASH 42.0 (36.6–43.7), with mean ALT 91 vs 23 (p < 0.001) and median CAP score 374 dB/m vs 278 dB/m with a trend towards raised median liver elastography 11.2 Kpa (IQR 6.6–11.5) vs 7.7 Kpa (IQR 5.7–10.0). In peripheral blood, there was significantly greater CXCR3+ expression in CD4+ T cells in NASH (MFI 5447 vs 4377, p < 0.05) with a trend towards increased interferon gamma expression following stimulation with PMA. Overall expression of the liver homing marker CXCR6 was increased across all peripheral T cells in NASH by multiple linear regression analysis (p = <0.05). In particular, there were significantly more CD4+CXCR6+ T cells in NASH versus non-NASH. Among CD45+ cells extracted from liver tissue, patients with NASH had significantly more cytotoxic CD8+ Tcells (p < 0.01). In the visceral adipose compartment, Th2 cells (CD4+CXTH2+) sampled from obese non-NASH patients had significantly higher levels of CXCR6 expression compared to patients with NASH. Conversely there was a trend towards higher expression of CXCR6 on Th1 cells (CD4+CXCR3+) sampled from patients with NASH compared to those without (p = 0.059)

Conclusion: To our knowledge, this is the first study of immune cell phenotype in multiple anatomical compartments in this patient group. We find evidence of a pro-inflammatory, liver-homing phenotype in peripheral blood and adipose tissue and a dominant type 1 immune phenotype in all 3 compartments. Further investigation of the role of the adaptive immune system in the pathogenesis of NASH is warranted.

SAT023
The influence of obesity, non-alcoholic steatohepatitis and bariatric surgery on plasma lipid profile
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Background and Aims: Obesity is often accompanied by non-alcoholic steatohepatitis (NASH). NASH is characterized by hepatic fibrosis, lipid accumulation and inflammation. Bariatric surgery (BS),
the gold standard treatment for obesity, has shown improvements in global health of obese individuals, but their effect on plasma lipid profile is still unknown. Our main aim was to assess changes in lipid profile of control population, obese patients with and without NASH and obese patients that underwent BS and were followed-up 12 months.

Method: Plasma samples were obtained from the participants and a lipid extraction was fulfilled. Then, we performed a lipidomic analysis by UHPLC-ESI-QTOF-MS. Results were compared in five different ways: healthy controls (n = 50) vs obese patients without NASH (n = 50) (obesity effect), obese patients with (n = 50) and without (n = 50) NASH (NASH effect), obese patients 12 months after BS (n = 50) vs obese patients with and without NASH (effect of BS in obese patients). Healthy individuals were also compared to obese patients 12 months after BS to assess possible restoration of healthy lipidome.

Results: Most lipid concentrations were statistically decreased in non-NASH obese patients than in healthy controls. Besides, obese patients with NASH had increased lipid concentrations compared to obese patients that were non-NASH. With that, we found few possible lipid candidates that could differentiate NASH from non-NASH, as seen in ROC curves of ChoE 18:1 and TG 50:1. However, multivariant analysis did not allow a complete distinction between groups. The effect of BS was different depending on the presence of NASH. If obese patients had NASH, BS altered much more lipid concentration than in obese patients that were non-NASH. Regarding obese patients and their follow-up after BS, we observed a different behaviour in the analysed lipid categories. Moreover, we observed that BS was not able to recover a healthy lipidome.

Conclusion: Obesity and mainly NASH are linked to a specific plasma lipidome. There are some lipids that are extremely different between obese patients with and without NASH that could lead to future non-invasive NASH biomarkers. Bariatric surgery improves clinical and biochemical characteristics of obese patients; however, it reduces plasma lipid concentrations even more than those concentrations found in healthy controls, probably due to the absorption modification after surgical intervention.

SAT024
Growth differentiation factor 11 promotes progression of non-alcoholic fatty liver disease
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Background and Aims: GDF11 (Growth Differentiation Factor 11) is a member of the TGF-beta superfamily and several recent papers implicated GDF11 as an antiaging factor. Nonetheless, its role in liver diseases is not fully clarified. Our aim was to evaluate the role of GDF11 in the progression of nonalcoholic fatty liver disease (NAFLD) to non-alcoholic steatohepatitis (NASH).

Method: We performed transcriptomic and lipidomic analyses in hepatoma cells treated with recombinant GDF11, to determine effected signaling pathways after GDF11 treatment. We administered recombinant GDF11 to ob/ob mice with NAFLD by daily intraperitoneal injection for 14 days to monitor the overall pathological changes in the liver. We also analyzed liver biopsies from a cohort of 33 morbidly obese Caucasian adults with biopsy-proven NAFLD (n = 20) or NASH (n = 13). We determined mRNA expression levels of GDF11 and other genes involved in NAFLD to NASH progression and we assessed correlations between obtained expression levels and clinico-pathological and histological features.

Results: In hepatoma cells, GDF11 treatment caused ALK5-dependent SMAD2/3 nuclear translocation, promoted accumulation of long acyl chain diacylglycerols and triacylglycerols and up-regulated TGF-beta activated genes involved in the deposition of extracellular matrix. In obese mice treated with recombinant GDF11 we observed...