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**Contribution of visceral fat and hepatic fat to metabolic derangements and liver damage in NAFLD patients.**

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# JOURNAL OF HEPATOLOGY

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alcohol consumption, in whom NAFLD was diagnosed by non enhanced CT and were compared to 33 healthy controls matched for age, and BMI. Tissue Doppler echocardiography (TDI) was performed in all patients.

**Results:** Patients with NAFLD were male (95% VS 72%,  $P < 0.01$ ) and had increased mean systolic blood pressure ( $140 \pm 14$  VS  $132 \pm 14$ ,  $P < 0.02$ ) than controls. NAFLD patients had lower early diastolic tissue velocity ( $e'$  on TDI,  $10.2 \pm 2.9$  cm/sec vs.  $12.2 \pm 3.1$  cm/s,  $P < 0.011$ ), lower ratio of early diastolic to late diastolic mitral inflow (E/A ratio  $1.12 \pm 0.4$  vs  $1.42 \pm 0.35$ ,  $P < 0.28$ ), higher atrial reversal velocity of mitral inflow (Ar velocity  $28 \pm 6$  vs  $25 \pm 4.4$ ,  $p < 0.03$ ), higher left ventricle mass ( $156 \pm 30$  VS  $137 \pm 31$ ,  $p < 0.013$ ), higher deceleration time (DT  $208.2 \pm 40$  ms vs  $184.2 \pm 26$ ,  $P < 0.004$ ), and higher short axis mediastinal fat (SAX  $6.7 \pm 2.9$  mm vs.  $5.1 \pm 2.6$ ,  $P < 0.019$ ) than healthy controls. All of these differences remained significant after adjustment for hypertension and other cardio metabolic risk factors. Pericardial fat thickness, left ventricular volumes, ejection fraction, and relation time (IVRT) were not different.

**Conclusions:** Our data show that patients with NAFLD have early features of LV diastolic dysfunction.

### 1349

#### PREDICTIVE VALUE OF EPICARDIAL FAT AS NEW MARKER OF METABOLIC SYNDROME AND EARLY VASCULAR DAMAGE IN PATIENT WITH NAFLD

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**Background:** Increased visceral adiposity is considered the hallmark of the metabolic syndrome (MS) and Non-alcoholic fatty liver disease (NAFLD). Epicardial adipose tissue has been implicated in the pathogenesis of coronary atherosclerosis.

**Aim:** To evaluate in patients with MS and NAFLD the threshold values of echocardiographic epicardial fat thickness and their association with a) metabolic and clinical parameters, b) early atherosclerotic vascular damage, by carotid intima media thickness (IMT).

**Methods:** 41 patients with MS and with clinic, laboratory, ultrasound, histology proven NAFLD were enrolled in the study (20 men, age  $48 \pm 13$  years, BMI  $33 \pm 5$  kg/m<sup>2</sup>, waist circumference (men)  $114 \pm 11$  cm, (women)  $109 \pm 10$  cm) and 20 controls without MS and without NAFLD (11 men, age  $47 \pm 9$  years BMI  $23 \pm 1$  kg/m<sup>2</sup>). Physical examination, blood tests, carotid ultrasound were performed. Epicardial fat thickness was evaluated by transthoracic echocardiogram.

**Results:** Patients with MS and NAFLD had significantly higher epicardial fat thickness than controls ( $4.95 \pm 2.6$  and  $2.69 \pm 1.8$  mm,  $p = 0.01$ ). Considering as increased values higher than 2.7 mm (median of controls) we evaluated variables associated with increased epicardial fat. Age, BMI, waist circumference, fasting glucose, HOMA-IR, IMT were significantly higher in subjects with increased epicardial fat than without, while the echocardiographic diastolic function index early/atrial peak flow (E/A) was significantly lower. At multivariate analysis HOMA-IR remained the independent variable associated with epicardial fat ( $p = 0.04$ , OR 1.8, 95% CI 1.037–3.58).

**Conclusion:** In conclusion patients with MS and NAFLD had higher value of epicardial fat thickness than controls, the increased epicardial fat values were associated with insulin-resistant and with early vascular damage. Epicardial fat measurement, an easy diagnostic tool to define visceral and cardiac adiposity could be proposed to better predict the cardiovascular risk and connection with NAFLD.

### 1350

#### GASTRIC BYPASS IS EFFICIENT ON METABOLIC AND LIVER STEATOSIS AFTER LAPAROSCOPIC GASTRIC BANDING RELAPSE

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For some morbid obese patients the benefit of gastric banding (GB) appears insufficient in terms of BMI and insulin resistance (IR) decrease. It is not known whether a switch to gastric bypass (GBP) may be proposed in such patients.

#### Aims:

1. To evaluate the evolution of patients considered as having an insufficient response to GB.
2. To determine effectiveness of the switch to GBP in such patients in term of BMI, insulin resistance and liver injury.

**Methods:** In a prospective database, 573 morbidly obese treated with GB were included. Clinical, histological and biological parameters (IR measured as  $1/QUICKI$ ) were recorded. Less-responder patients (LR) were treated at their request by GBP after exhaustive and careful selection.

#### Results:

1. Among 573 patients, 48 patients had a second line with GBP for insufficient response. 525 were not considered for a second line as response was considered as satisfactory by patient and physician.

LR Patients treated by GBP were not significantly different at baseline from the 525 in terms of: age (39.8 vs 40.2 years), steatosis (30 vs 25%),  $NAS \geq 3$  (27.3 vs 27.3%), cholesterol (5.2 vs 5 mmol/l) GGT (26 vs 30 IU/l), IR (3.1 vs 3.1). Whereas LR patients were significantly different for BMI (47 vs 45.1 kg/m<sup>2</sup>  $p = 0.005$ ), ALT (21 vs 26  $p = 0.03$ ), triglycerid (1.6 vs 1.4  $p = 0.03$ ).

Insufficient response to therapy was confirmed by the fact that steatosis score and IR return close to the value observe at baseline. Whereas the other had a lower amount of steatosis 3%, IR 2.83 at five years ( $p = 0.004$ ).

2. The evolution of patients after the switch for GBP, LR patient treated with GBP observe a improvement in BMI ( $-18\%$   $p = 0.003$ ), decrease in IR from 2.94 to 2.7  $p = 0.003$ , steatosis from 30% to 5%  $p < 0.05$ . The benefit was sustained at 5 years as shown by a lower steatosis (1%) and IR (2.64) ( $p < 0.05$  as compared to baseline).

**Conclusion:** Fat amount and IR return to baseline values in LR patients. Switch to GBP seems to restore response to bariatric surgery. These data support the need for alternative strategy to GB.

### 1351

#### CONTRIBUTION OF VISCERAL FAT AND HEPATIC FAT TO METABOLIC DERANGEMENTS AND LIVER DAMAGE IN NAFLD PATIENTS

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**Background and Aims:** Both hepatic and visceral fat have been implicated in the onset and progression of metabolic syndrome and NAFLD. However, their relative role is still debated. Aim of this study was to determine the relative contribution of hepatic and visceral fat to both metabolic derangements and histological liver damage in subjects with biopsy-proven NAFLD.

**Methods:** In 22 non-diabetic, non-dyslipidaemic patients with biopsy-proven NAFLD we measured whole abdomen visceral fat (VF) by MRI, fasting endogenous glucose production (EGP) and lipolysis by tracer infusion, peripheral insulin resistance (IR) as HOMA, Hepatic-IR as EGP x fasting insulin, and adipose tissue (Adipo)-IR as basal FFA levels x fasting insulin. Hepatic histology was scored according to Kleiner, liver fat was also reported as percentage (LF%).

**Results:** In our study cohort, VF was increased in proportion to BMI ( $r=0.54$ ,  $p<0.004$ ) and to LF%, ( $r=0.43$ ,  $p<0.03$ ), whereas LF% was not correlated with BMI. Only LF%, but not VF, was associated with circulating FFA levels ( $r=0.51$ ,  $p<0.01$ ), and Adipo-IR ( $r=0.41$ ,  $p<0.05$ ), while no correlation was found between either LF% or VF with Hepatic-IR or HOMA.

Patients with NAS score  $\geq 4$  (compared to those with NAS 0–3) had more VF ( $3.9\pm 0.7$  vs  $2.8\pm 0.4$  kg), increased FFA concentrations ( $525\pm 52$  vs  $804\pm 98$  mmol/l), peripheral IR (HOMA:  $3.7\pm 0.5$  vs  $2.8\pm 0.8$ ), hepatic-IR ( $169\pm 23$  vs  $124\pm 32$ ), and adipose-IR ( $13.2\pm 2.5$  vs  $6.3\pm 1.8$ ) (all  $p<0.05$ ). When taking into account only ballooning and lobular inflammation in the NAS score, we found that subjects with a composite score  $>2$  had an impaired suppression of lipolysis.

Compared to patients without fibrosis, those with fibrosis had more VF ( $3.9\pm 0.6$  vs  $2.7\pm 0.7$  kg,  $p<0.03$ ), but not LF%, and no differences were found in the indexes of IR.

**Conclusions:** In NAFLD subjects, liver fat is associated with metabolic derangements and insulin resistance, but insulin resistance of the adipose tissue and VF accumulation appear to provide a major contribution to liver damage.

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### 1352

#### INTEROBSERVER CONCORDANCE IN CONTROLLED ATTENUATION PARAMETER (CAP) MEASUREMENT, A NOVEL TOOL FOR THE ASSESSMENT OF HEPATIC STEATOSIS BASED ON TRANSIENT ELASTOGRAPHY

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**Introduction:** The combination of transient elastometry (TE) with controlled attenuation parameter (CAP) allows non-invasive measurements of hepatic steatosis (HS) simultaneously to liver stiffness. TE is characterized by a high reproducibility and low inter-observational variability in HCV-infected patients with or without HIV coinfection. Nevertheless, no data are available on interobserver differences in CAP values. This is a relevant point, since HS is a very common disorder among HIV-infected patients, and accurate non-invasive diagnosis is critical.

**Objective:** To assess the concordance of CAP measurements between two independent observers in patients infected with HIV and/or hepatitis virus.

**Methods:** In a cross-sectional, prospective study conducted from December 2011 to March 2012 in a university hospital in Spain, CAP-enabled TE acquisitions were performed by two independent observers in 118 consecutive patients with HIV and/or hepatitis virus infection. The interobserver concordance between the CAP value measurements was assessed using the intraclass correlation coefficient (ICC) and the concordance of the classification of patients regarding the grades of HS was characterized using the kappa index. Patients with CAP  $\geq 238$  dB/m were considered to bear significant HS ( $\geq 10\%$  hepatocytes involved), as previously reported.

**Results:** 78% patients were male. Twenty (17%) patients were HIV monoinfected, 44 (37.3%) hepatitis C virus (HCV)-monoinfected and 52 (44%) showed HIV/HCV coinfection. The median (Q1–Q3) values of CAP obtained by the first and the second observer were 228 (205–265) and 227 (196–269) dB/m, respectively. The median (interquartile range) of the absolute difference of CAP values between the two observers was 20 (10–41) dB/m. The overall ICC was 0.84 (95% confidence interval: 0.77–0.88). The kappa index for the concordance of classification for the presence of significant HS was 0.55. No factor was associated with a greater concordance between observers.

**Conclusions:** The concordance of CAP values obtained by two observers is good. Therefore, the determination of HS by means of CAP in HIV and/or hepatitis virus infection represents an observer-independent and easily performable method. However, the concordance of the diagnosis of significant HS, defined by the cutoff of 238 dB/m, is suboptimal.

### 1353

#### EFFECTS OF OMEGA-3 POLYUNSATURATED FATTY ACIDS (PUFA) FROM FISH AND FLAXSEED OILS ON NONALCOHOLIC STEATOHEPATITIS (NASH)

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**Introduction:** There are very few intervention strategies that have been proven in non-alcoholic fatty liver disease (NAFLD). Omega-3 polyunsaturated fatty acids (PUFA) seem to be efficacious on NAFLD treatment from experimental models, but few randomized trials have been realized. The aim of this study was to evaluate prospectively the efficacy of Omega-3 PUFA derived from fish and flaxseed in non-alcoholic steatohepatitis (NASH) patients.

**Methods:** Sixty patients with biopsy proven NASH were included in the randomized placebo controlled trial. The patients were randomized into two groups. Omega-3 group ( $n=30$ ) received capsules containing 945 mg of Omega-3 PUFA [ $\alpha$  linolenic acid/64%, eicosapentaenoic acid (EPA)/16% and docosahexaenoic acid (DHA)/21%], in 3 capsules/day. Placebo Group ( $n=30$ ), received 3 placebo capsules containing mineral oil. The intervention was carried out for 6 months, when patients were re-submitted for new liver biopsy. Primary endpoint was liver histology according to the NASH activity score (NAS) at baseline and 6 months. Second endpoints were evaluated by analysis of serum aminotransferases, fasting lipid profile, serum glucose, anthropometric parameters and serum levels of cytokines at 0, 3 and 6 months.

**Results:** These 60 patients enrolled, 10 were not finished the study (5 in Omega-3 group and 5 in the Placebo group). Concerning the primary endpoint, the NAS activity improved by 57% in the placebo group and 67% in the omega-3 group, however, no significant difference was seen ( $p=0.33$ ), the hepatocellular ballooning reduced 22% in the placebo group and 33% in the omega-3 group, also with no difference between groups ( $p=0.28$ ). Omega-3 did not reduce steatosis, lobular inflammation and fibrosis. Serum aminotransferases, fasting lipid profile, serum glucose, anthropometric parameters and serum levels of IL-6 and TNF- $\alpha$  were not altered with the treatment.

**Conclusion:** Our results indicate that Omega-3 PUFA from fish and flaxseed oil compound cannot improve, after 6 months, the liver histology, biochemical parameters and serum levels of IL-6 and TNF- $\alpha$ . The limitations of this study were the small number of patients enrolled and the composition of Omega-3 compound that was enriched with linolenic acid (64%) than EPA/DHA. Further study is needed to confirm these results.