SUBJECTS WITH NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD) DISPLAY INCREASED VISCERAL AND PANCREATIC FAT ASSOCIATED WITH WORSE METABOLIC PROFILE

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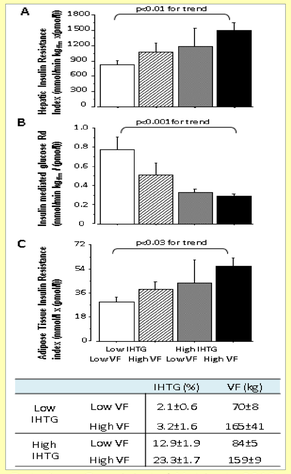
Background

Together with insulin resistance (IR), lipotoxicity and inflammation, patients with non-alcoholic fatty liver diseases (NAFLD) often show increased visceral fat (VF) that correlate with the amount of hepatic fat (IHTG). We have previously shown (Fig.1) that IR measured at the level of muscle, liver and adipose tissue, is increased proportionally to both VF and IHTG.

Beyond VF and HF, fat can also accumulate in the pancreas (PF) leading to impaired insulin secretion and increasing the risk of diabetes (T2DM).

If VF is playing a key role in the progression of liver dysfunction is not clear. In addition if NAFLD patient have also increased pancreatic fat has not been evaluated.

IR is increased proportionally to both VF and IHTG



		IHTG (%)	VF (kg)
Low IHTG	Low VF	2.1±0.6	70±8
	High VF	3.2±1.6	165±41
High IHTG	Low VF	12.9±1.9	84±5
	High VF	23.3±1.7	159±9

Data from Gaggini et al Nutrients 2013, and Gastaldelli et al Gastroenterology 2007.

Aims:

The aim of this work was to quantify, by magnetic resonance (MR), the amount of visceral, hepatic and pancreatic fat in patients with proven NAFLD and evaluate the impacts on parameters of liver damage, lipid profile and metabolic alterations.

Methods:

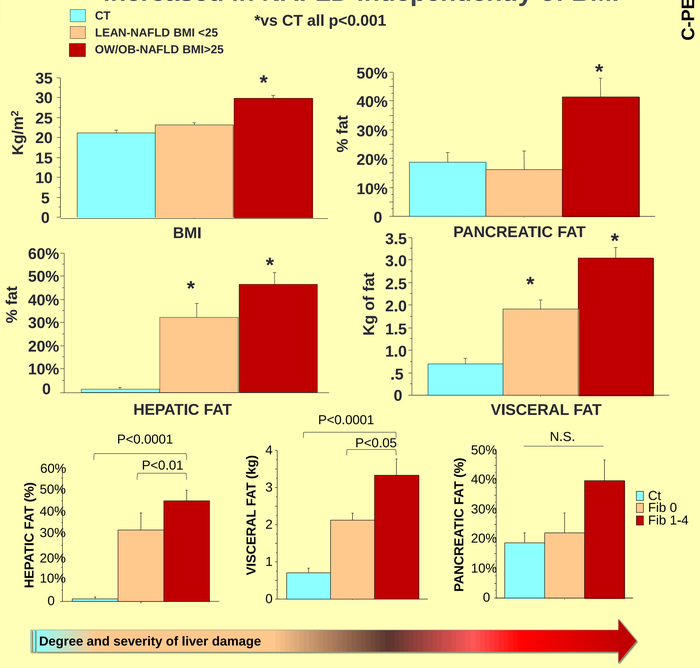
We studied 34 non diabetic subjects with biopsy proven NAFLD (scored according to Kleiner) and 8 healthy controls (CT). In all subjects we measured plasma concentrations of triglycerides (TG), free fatty acids (FFA), insulin, C-peptide, monocyte chemoattractant protein-1(MCP-1) and adiponectin, FFA composition by gas chromatography mass spectrometry (GCMS), visceral, hepatic and pancreatic fat by magnetic resonance imaging (MRI). In addition we evaluated lipolysis and endogenous glucose production (EGP) using tracer infusion. We then calculated indexes of resistance (IR): HOMA, Adipo-IR (Lipolysis x Insulin) and hepatic IR (Hep-IR= EGP x Insulin).

Results:

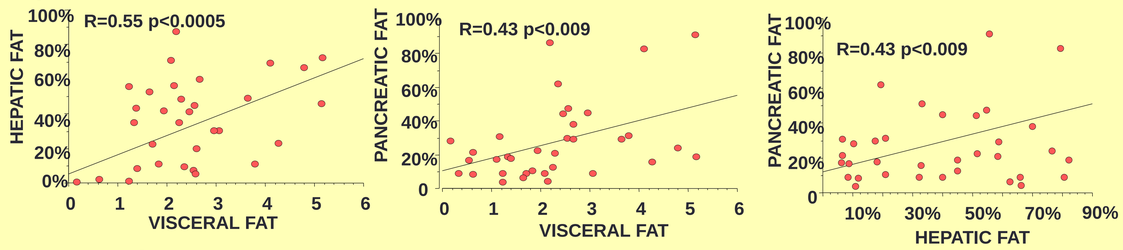
Clinical characteristics of the subjects

	Control (n=8)	*NAFLD BMI<25 (n=10)*	*NAFLD BMI>25 (n=24)*
Gender M/F	4/4	2/8	5/20
BMI (Kg/m²)	21.22±0.58	23.17±0.58	29.98±0.62*
ALT (U/l)	16.25±1.57	57.70±6.26*	83.08±7.99*
AST (U/l)	19.62±1.57	35.80±5.31	49.44±8.04*
GGT (U/l)	14.25±4.22	155.10±34.88*	84.60±24.32
GLU 0 (mg/dL)	90.75±1.98	94.80±2.55	98.08±2.67
Insulin (mU/L)	5.94±0.64	8.95±0.89	14.66±1.37*
TG (mg/dL)	56.12±6.56	90.10±7.01	111.80±12.56*
FFA (mmol/L)	0.61±0.06	0.59±0.04	0.66±0.06
LDL (mr/dL)	108.50±7.71	131.80±12.46	127.36±6.01
HDL (mg/dL)	55.00±4.74	51.30±3.90	42.80±2.58*
Total Cholesterol (mg/dL)	169.75±5.79	202.10±10.38	190.00±7.56

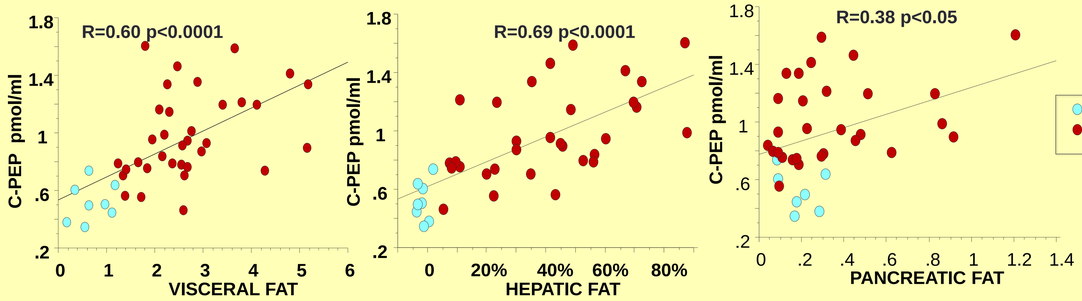
Hepatic and visceral fat, not pancreatic fat, are increased in NAFLD independently of BMI



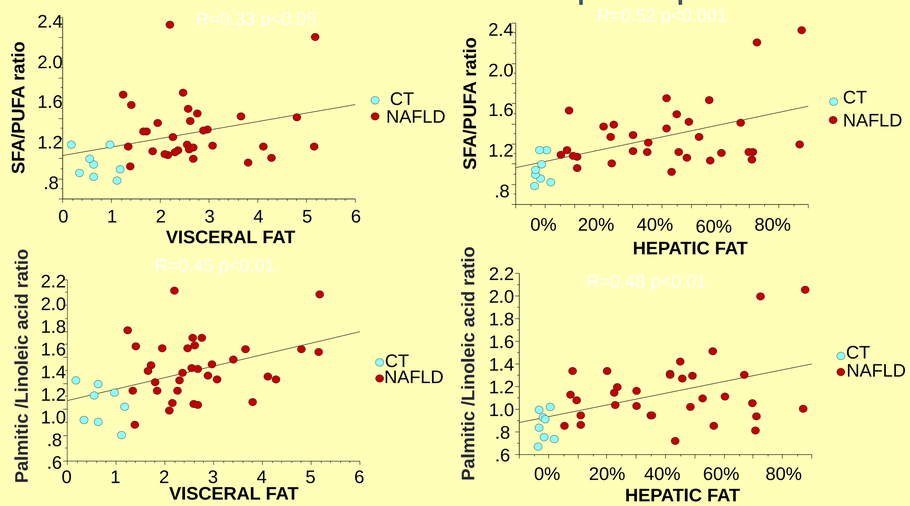
Visceral fat was associated with both hepatic and pancreatic fat accumulation in patients with NAFLD



Visceral, hepatic and pancreatic fat are associated with increased insulin secretion



VF and HF are associated with alterations in lipid composition



Summary and Conclusions

In patients with NAFLD, beside hepatic fat also visceral and pancreatic fat are associated with an adverse lipid and inflammatory profile. Thus, not only hepatic but also VF and pancreatic fat are major risk markers of metabolic derangement in NAFLD and can predict the progression of liver disease and liver damage.

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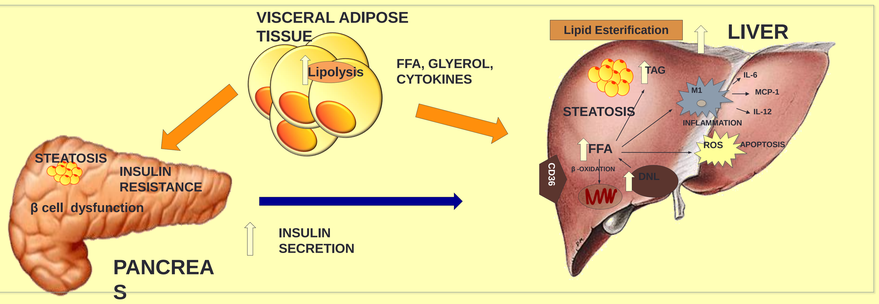

In the whole group, HF correlated with both VF (r=0.47) and PF (r=0.41). HF and VF correlated positively with high C-peptide and insulin (all r>0.4; all p<0.05), HOMA, Hep-IR and Adipo-IR (all r>0.4; all p<0.05), parameters of lipotoxicity (palmitic/linoleic acid ratio, SFA/PUFA) (all r>0.3; all p<0.05) and inflammation (MCP-1) (both r>0.5; both p<0.01) and inversely associated with adiponectin (both r>0.5; both p<0.001) while PF correlated only with C-peptide (i.e., pre-hepatic insulin secretion).