Differences in insulin sensitivity and adipose tissue distribution in obese subjects – is there a benign form of adiposity?

J. Machann[1], N. Stefan[2], N. Schwenzer[1], F. Springer[1], H-U. Häring[2], C. Claussen[3], A. Fritsche[2], and F. Schick[1]
[1]Section on Experimental Radiology, University Hospital Tübingen, Tübingen, Germany, [2]Department of Internal Medicine IV, University Hospital Tübingen, Tübingen, Germany, [3]Department for Diagnostic and Interventional Radiology, University Hospital Tübingen, Tübingen, Germany

Introduction

Obesity and its concomitant diseases as Type 2 Diabetes (T2D) and cardiovascular diseases are of dramatically increasing prevalence worldwide and describe a major burden for healthcare costs [1]. Adiposity is defined by a body mass index (BMI, calculated as the ratio between weight (kg) and height (m) squared) higher than 30 kg/m². However, there are obese subjects which are characterized by normal insulin sensitivity on the one hand (insulin sensitive subjects, IS) and insulin resistant subjects (IR), which describes a pre-stage of T2D. Aim of this cross-sectional analysis was to determine differences in adipose tissue distribution and ectopic lipids in liver and skeletal muscle in order to define a kind of "benign adiposity" in subjects with BMI > 30kg/m².

Material and Methods

In total, 144 volunteers at increased risk for T2D (90 females, 54 males) were included in this analysis. For determination of total body adipose tissue (AT) distribution and quantification of different AT compartments, a TSE sequence was applied on a 1.5T whole-body imager (Magnetom Sonata, Siemens Healthcare, Germany). Measurement parameters were: TE/TR=12ms/490ms, slice thickness 10mm, 10 mm gap between the slices) [1]. A total of 100-130 images were obtained from fingers to toes from each volunteer in prone position. Post-processing was performed by a semiautomatic segmentation procedure [2]. Following parameters were assessed: Total adipose tissue (TAT), visceral adipose tissue (VAT) and subcutaneous abdominal adipose tissue ($SCAT_{abd}$), adipose tissue of the lower extremities (AT_{LE}) ranging from feet to head of femur, adipose tissue of upper extremities (AT_{UE}) ranging from head of humerus to fingers. All AT parameters are given as percent body weight (%bw). Single voxel MRS (STEAM) with a short TE of 10 ms was applied in liver (TR = 4 s) and skeletal muscle (TR = 2 s) for determination of hepatic lipids (HL), calculated as the ratio between lipids (methylene and methyl resonances) and water, and intramyocellular lipids (IMCL) in tibialis anterior and soleus muscle of the right lower leg, given as the ratio between methylene resonance of IMCL and methyl signal of creatine. Insulin sensitivity was estimated by an oral glucose tolerance test (oGTT, ISI Matsuda in a.u.) which was performed immediately after the MR examination. Subjects were divided in two groups – insulin sensitive (IS) and insulin resistant (IR), separated by the median of ISI Matsuda.

Results

Anthropometric data, ISI Matsuda and adipose tissue volumes are given in Table 1. There is no significant difference in age, BMI and %TAT between the IS and IR – neither in females, nor in males. In females, %VAT is significantly higher in the IR group, in males, this difference is pronounced but fails statistical significance (p=0.07). $SCAT_{abd}$ is very similar for IR and IS in both, obese females and males. $\%AT_{LE}$ shows an interesting feature for both gender groups as it is significantly higher for the IS ones. AT_{UE} is significantly higher in IR females and slightly lower in IR males compared to the IS ones. Hepatic lipids are more than doubled in IR for males and females ($p<0.001$ for both). $IMCL_{TA}$ are also significantly increased in IR obese subjects whereas $IMCL_{SOL}$ are almost identical in males and slightly higher in IR females. Figure 1 shows exemplary axial images from the umbilical level of an insulin sensitive male subjects (46 years-old, BMI 32.9kg/m², ISI Matsuda: 13.8 a.u., left column) and an obese insulin resistant male subject (50-years-old, BMI 32.2kg/m², ISI Matsuda 2.9 a.u., right column) and the corresponding spectra from the liver (lower row). It can be seen that the IR subject has clearly lower $SCAT_{abd}$ and higher VAT compared to the IS subject. Furthermore, the IS subject has HL<1% whereas the IR subject has approx. 25% HL.

Discussion

From these cross-sectional data it could be shown that subjects with identical body mass index (BMI) may differ in their adipose tissue distribution and ectopic lipid content. As a result, the lower in the body the adipose tissue is located, the better for the metabolic parameters as expressed by insulin sensitivity. It is well known that visceral adipose tissue and hepatic lipids are indicators for insulin sensitivity and higher VAT and HL correlate with insulin resistance – however, a differentiation between "good" and "bad" adiposity can be shown from these data. This also goes in line with longitudinal data in [3] where it is shown that subjects with low baseline VAT and HL will benefit from a lifestyle intervention whereas subjects with high VAT and HL don't. The onset of VAT and HL accumulation remains speculative, but our data clearly show that BMI alone is not a good measure for obesity in terms of metabolic alterations.

References

1. Artham SM et al. J Cardiometab Syndr 2008; 3:155-161.
2. Machann J et al. J Magn Reson Imaging 2005; 21:455-462.
3. Machann J et al. Radiology 2010; 257:353-363.

Acknowledgements

Supported by the Deutsche Forschungsgemeinschaft (DFG, KFO 114)

	females			males		
	IS	IR	p	IS	IR	p
n	45	45		27	27	
ISI Matsuda / a.u.	15.2±5.2	5.8±1.6		13.2±6.3	4.9±1.7	
age / years	47.2±11.6	45.7±11.2	n.s.	42.0±13.8	46.4±12.8	n.s.
BMI / kg/m²	33.4±2.9	34.4±2.7	n.s.	33.9±3.8	34.6±4.2	n.s.
TAT / %bw	48.9±3.8	48.4±4.8	n.s.	38.1±5.7	36.6±5.3	n.s.
VAT / %bw	3.3±1.6	3.9±1.1	0.02	5.2±1.7	5.9±1.8	n.s.
$SCAT_{abd}$ / %bw	19.6±2.8	20.0±2.5	n.s.	14.6±3.2	14.0±3.1	n.s.
AT_{LE} / %bw	20.3±3.2	18.2±3.2	0.002	13.7±3.3	12.3±2.5	0.04
AT_{UE} / %bw	5.7±1.0	6.3±1.2	0.01	4.7±0.8	4.4±0.9	n.s.
HL	5.2±5.4	12.8±11.5	0.0001	6.9±5.3	16.5±12.0	0.0003
$IMCL_{TA}$	4.0±1.6	4.8±1.7	0.02	3.0±1.3	4.6±1.6	0.0004
$IMCL_{SOL}$	15.9±8.7	17.5±10.1	n.s.	17.3±10.5	17.4±5.9	n.s.

Table 1: *Anthropometric data, metabolic characteristics, adipose tissue compartments and ectopic lipids of the obese study cohort.*

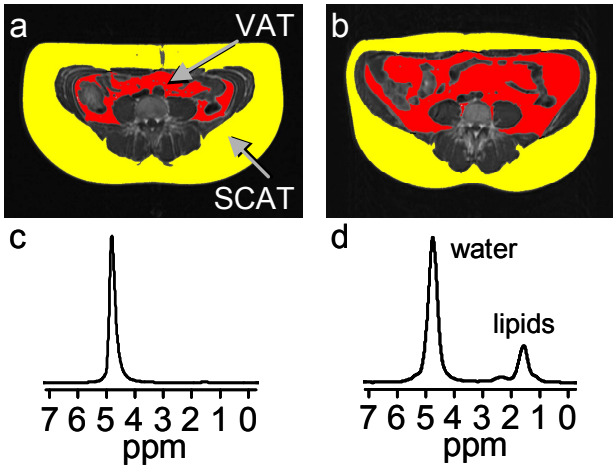

Figure 1: *Axial T1-weighted images at the umbilical level of an insulin sensitive (a) and an insulin resistant volunteer (b) with comparable BMI. (c) and (d) show the corresponding spectra recorded in segment 7 of the liver. Insulin sensitive volunteer (left row) has clearly lower VAT and HL compared to the insulin resistant subject (right row).*