

Relevance of visceral adipose tissue and intrahepatic lipids in the pathogenesis of insulin resistance – a cross-sectional study

J. Machann¹, C. Thamer², B. Schnödt¹, N. Stefan², H-U. Häring², C. D. Claussen³, A. Fritsche², F. Schick¹

¹Section on Experimental Radiology, Tübingen, Germany, ²Department of Endocrinology, Metabolism and Pathobiochemistry, Tübingen, Germany, ³Department of Diagnostic Radiology, Tübingen, Germany

Introduction

Obesity is the most important risk factor in the pathogenesis of insulin resistance and type 2 diabetes [1,2]. However, not only the amount of whole body adipose tissue (PFAT) but also its distribution play an essential role. Besides the professional fat cells in subcutaneous and visceral adipose tissue, the so-called ectopic fat in organs which normally do not contain fat at all but are affected by insulin resistance, e.g. the liver, are of major interest. Magnetic resonance imaging (MRI) and spectroscopy (MRS) offer an excellent tool for non-invasive determination of different lipid compartments and even quantification of small amounts of intrahepatic lipids (IHL) [3,4]. Aim of the present study was quantification of visceral adipose tissue (VAT) and IHL in a cohort at increased risk for type 2 diabetes and correlation with insulin sensitivity.

Material and Methods

One hundred eighty healthy volunteers (105 females, 45±11 years, 75 males, 47±11 years) were recruited in the framework of the TULIP-study (Tübingen Lifestyle Intervention Program) due to increased risk for type 2 diabetes. Inclusion criteria were obesity (body mass index BMI > 27 kg/m²), and/or impaired glucose tolerance, and/or family history of diabetes, and/or gestational diabetes. All volunteers underwent MRI/MRS for quantification of adipose tissue compartments and a hyperinsulinemic glucose clamp for determination of insulin sensitivity. MR examinations were performed in the early morning after an overnight fasting period on a 1.5 T whole body imager (Magnetom Sonata, Siemens, Erlangen, Germany). For determination of total body adipose tissue distribution, a TSE sequence was applied (TE/TR=12ms/490ms, slice thickness 10mm, 10 mm gap between the slices). A total of 100-130 images was obtained from each volunteer. Postprocessing was performed by semiautomatic segmentation of lean tissue and adipose tissue. VAT was selected manually from abdominal images (see lower images in Fig. 1a,b). For determination of IHL a single voxel STEAM technique was applied in segment 7 of the liver with TE/TR=10ms/4s, VOI (3x3x2)cm³, 32 acq. (see Fig. 1c). Signal integrals of water and lipids were quantified in fixed frequency intervals. IHL are given as percentage value using the water signal as internal reference.

Results

BMI did not show significant differences between males and females (30.1±4.0 kg/m² in males, 28.7±5.1 kg/m² in females). However, females have significant higher PFAT compared to males (35.4±6.6% in females, 26.4±6.3 in males, $p < 0.001$). Males are characterized by significantly higher VAT (5.0±1.8l in males, 2.3±1.4l in females, $p < 0.001$) and slightly higher IHL (8.2±7.6% in males, 5.4±7.7% in females, n.s.). Due to these differences, correlation between lipid compartments and insulin sensitivity was performed separately for males and females. Figure 2 shows the linear correlations between insulin sensitivity index (ISI) and VAT (Fig. 2a) and IHL (Fig. 2b). Data were log-transformed before statistical analysis to achieve normal distribution. Both lipid compartments reveal excellent negative correlation for females ($r = -0.61$ each) and are also highly correlated in males ($r = -0.40$ and $r = -0.51$).

Discussion

MRI and MRS offers excellent techniques for a reliable quantification of different lipid compartments in the human body. In the pathogenesis of insulin resistance, mainly the visceral adipose tissue (VAT) and the hepatic lipids (IHL) play an essential role as shown by the excellent correlation with insulin sensitivity. Furthermore, visceral adipose tissue seems to be an important predictor of hepatic lipid content. These detailed analyses might bring new information in the understanding of development of type 2 diabetes, which is an increasing world-wide problem.

References

1. World Health Organization, WHO Technical Report Series 894 (2000)
2. Hedley AA et al., JAMA 291: 2847-2850 (2004)
3. Machann J et al., JMIR 21:455-462 (2005)
4. Machann J et al., MAGMA 18 : 128-137 2005

Acknowledgements

Supported by a grant from the Deutsche Forschungsgemeinschaft (KFO 114/1)

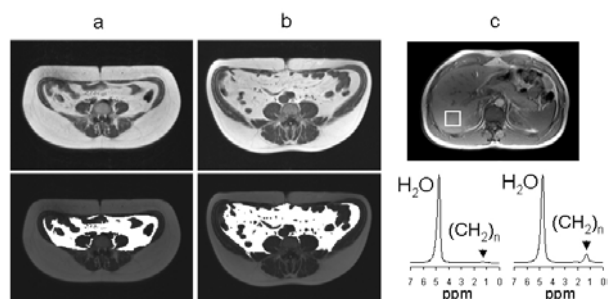


Fig. 1: T1-weighted images at the height of the umbilicus and principle of segmentation of VAT in a female (a) and a male (b) volunteer. (c) Typical spectra from the liver showing small amounts of IHL (methylene component, $(CH_2)_n$).

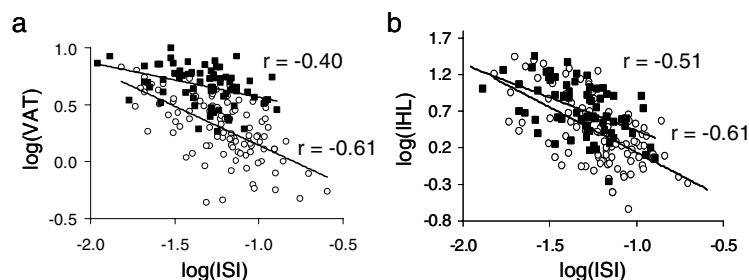


Fig. 2: Linear correlation between insulin sensitivity index (ISI) and visceral adipose tissue, VAT (a), and intrahepatic lipids, IHL (b) for males (squares) and females (circles).