Myocardial lipids and myocardial function in insulin resistant population.

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Background and Aims:
Impaired glucose metabolism is an independent risk factor for cardiovascular disease and heart failure. Results of non-invasive quantification of myocardial lipid accumulation by localized ^{1}H MR spectroscopy have recently suggested possible correlations between myocardial steatosis, myocardial function and impaired glucose metabolism in type 2 diabetic patients [1,2]. Furthermore, insulin resistance is associated with enhanced ectopic lipid accumulation in skeletal muscle and liver. Therefore, the aim of the present study was to assess relations between insulin resistance and myocardial lipid accumulation and function in non-diabetic women and compare them with women with manifested type 2 diabetes mellitus.

Material and Methods:
Up to now nine non-diabetic insulin sensitive (IS), ten metabolically matched insulin resistant (IR) as well as nine type 2 diabetes mellitus (T2DM) women underwent the functional and metabolic cardiac MR examination on a 3T Tim Trio MR System (Siemens Healthcare, Erlangen, Germany). In non-diabetic women (IR and IS) insulin sensitivity was assessed by oral glucose tolerance test and subsequent calculation of the Clamp-Like Index[3]. Metabolic characterization of the study participants is given in the Tab. 1.

	IS	IR	T2DM
n	9	10	9
Age [y]	50 ± 5	50 ± 6	51 ± 8
BMI [kg.m^{-2}]	25 ± 2	28 ± 3	28 ± 2
CLIX	9.7 ± 0.7	4.5 ± 0.4	-
HbA1c [%]	5.4 ± 0.3	5.5 ± 0.3	9.2 ± 1.8$^{\#}$
TGs [mg/dl]	83 ± 20	105 ± 17	306 ± 282$^{\#}$
Cholesterol [mg/dl]	210 ± 32	226 ± 35	233 ± 66
HDL [mg/dl]	68 ± 16	67 ± 10	45 ± 13$^{\#}$
LDL [mg/dl]	126 ± 29	138 ± 28	141 ± 42
Heart rate [bpm]	64 ± 7	70 ± 8	73 ± 10
BP [mm Hg]	120/78	119/81	142/83

Tab 1. Metabolic characteristics of study population. (# p<0.05)

Visualization of cardiac function was performed using prospective ECG-gated cine TrueFISP sequences in 2-chamber, 4-chamber and short axes orientation. Short axes images were used to quantify left ventricular (LV) global (end-diastolic and end-systolic volume, stroke volume, ejection fraction and myocardial mass) via ARGUS software (Siemens Medical, Erlangen, Germany). Additionally FLASH-based prospective ECG-gated cine phase velocity encoding sequence was used to determine E/A ratio of mitral inflow as a measure of left ventricular diastolic function. Breath movement navigated and ECG triggered localized ^{1}H single voxel MR spectroscopy (PRESS; TE= 30ms) was used to measure myocardial lipid accumulation in ventricular septum of study participants. Repetition time of the sequence was given by the frequency of breath movement of individual volunteer and ranged from 2.5 to 7 s. An additional spectrum without water suppression (NS= 8) was used as the internal concentration reference. The spectra were processed by the Spectroscopy Processing tool within Syngo VB15 user interface provided by system manufacturer. The myocardial lipid content was be calculated as a ratio of the sum of intensities of (CH2)n (1.25 ppm) and CH3 (0.8-0.9 ppm) group resonances to the intensity of the water resonance from non-water suppressed spectra of the same VOI. Intensities of lipid and water resonance lines were corrected for T1- and T2- relaxation using individual repetition time and already published relaxation times of skeletal muscle at 3T[4]. Data are given as mean±SD and were analyzed by ANOVA (Bonferroni test and Dunnet t test).

Results:
Typical ^{1}H MRS spectra of ventrical septum is shown in the Fig 1. and detailed results of the study regarding the myocardial function and myocardial lipid accumulation are shown in Tab. 2. In general, no difference was found between IS and IR group, but a lower end-diastolic volume (p= 0.02 vs. IS), stroke volume (p= 0.002 vs. IS) and E/A ratio (p =0.023 vs. IR) was observed in the T2DM. Similarly only T2DM group presented with increased myocardial lipid accumulation (p= 0.034). Additionally, cardiac output tended to be lower in T2DM (p= 0.066 vs. IS)

Conclusion:
Our results suggest that increased myocardial lipid content and restricted myocardial capacity are not linked to insulin resistance per se, but might develop after the manifestation of type-2 diabetes.

Grant support: Austrian National Bank to M.K. - Jubiläumsfond # 13249 **References:** [1] McGavock et al. Circulation 2007; 116:1170-5. [2] Rijzewijk et al. J Am Coll Cardiol 2008; 52:1793-9.[3] Anderwald et al. Diabetes Care 2007; 30:2374-80 [4] Krssak et al. MAGMA 2004;16:155-9.

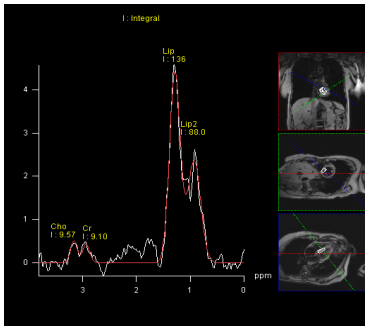

Fig 1. ^{1}H MRS spectrum of ventricular septum of healthy volunteer. Resonances of choline (Cho), creatine (Cr) and lipids (CH_2 – Lip, CH_3 – Lip2) are assigned.

	IS	IR	T2DM
LV – eject. f. [%]	71 ± 6	69 ± 7	69 ± 9
End syst. vol [ml]	32 ± 13	30 ± 12	26 ± 13
Card output [ml/min]	5.1 ± 0.8	4.8 ± 1.1	4.2 ± 0.8
End diast. vol [ml]	111 ± 19	96 ± 26	81 ± 24$^{\#}$
Stroke volume [ml]	79 ± 9	66 ± 16	55 ± 13 $^{\#}$
E/A - mitral flow	1.4 ± 0.3	1.6 ± 0.7	1.0 ± 0.4 $^{\#}$
Myoc. Lip. [% of WS]	0.42 ± 0.25	0.36 ± 0.18	0.68 ± 0.33$^{\#}$

Tab. 2. Myocardial function and lipid accumulation (# p<0.05)