Epicardial adipose tissue in children is associated with an unfavorable cardiometabolic risk profile, but is not a stronger indicator than BMI

Schusterova I., Joppova E., Stromplova D., Fatulova N., Tohatyova A., Leenen, F.*

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International Conference on Pediatric Cardiology
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THE GLOBAL OBESITY THREAT

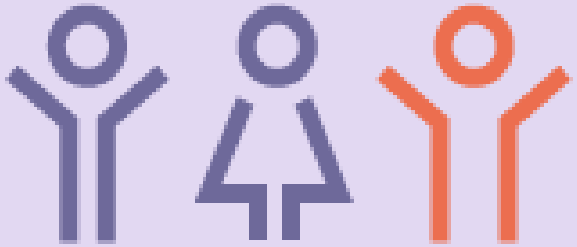
OBESITY AND OVERWEIGHT INCREASING WORLDWIDE



3.4 million

DEATHS CAUSED by overweight AND OBESITY

Obesity and overweight
INCREASED
27.5% IN ADULTS
47.1% IN CHILDREN
SINCE 1980



1 IN 3 CHILDREN

are overweight or obese

0

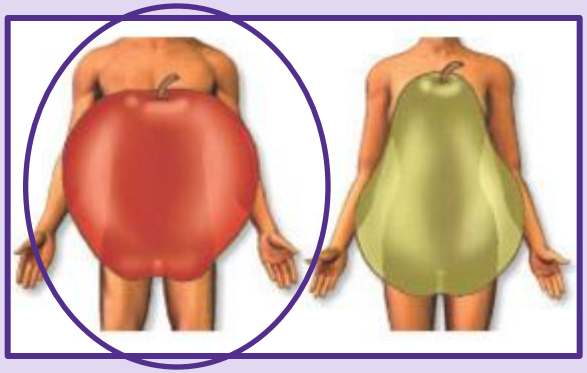
Number of countries succeeding in decreasing obesity in last 33 years

IHME
Institute for Health Metrics and Evaluation

World Health Organization

ANDROID TYPE OF OBESITY

- ***Fat excess primarily in abdominal wall and visceral mesentery***
- **Central obesity → clinical marker for *adiposopathy* ('sick fat') =** adipose tissue dysfunction promoted by positive caloric balance and sedentary lifestyle in genetically and environmentally susceptible individuals



- **DG criterion of *metabolic syndrome* (MS) → *cluster of CV RF* in association with insulin resistance (IR)**
- **↑ mortality**

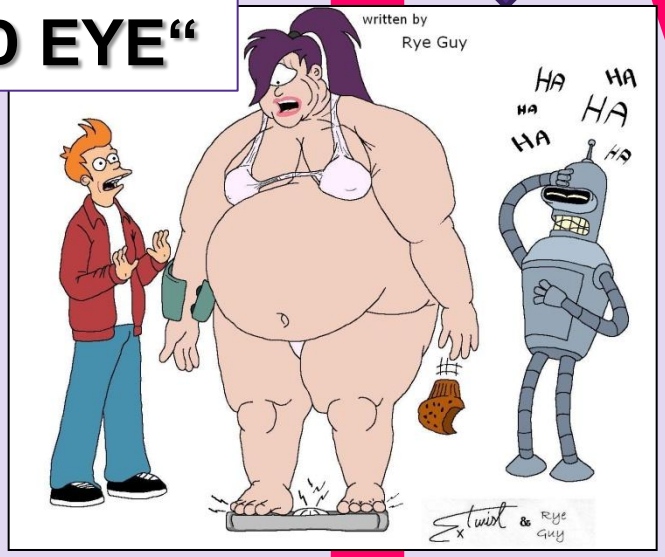
Poirier P. et al. *Arterioscler Thromb Vasc* Biol 2006; Fang J. et al. *JAMA* 2000; Kuk J. L. et al. *Obes Res* 2006; Bays, H.; *Curr Opin Endocr Diabetes Obes*, 2014.

ASSESSMENT OF OBESITY

BODY WEIGHT



„WITH THE NAKED EYE“



SUBCTUN. FAT



EPICARDIAL ADIPOSE TISSUE

BMI =BODY MASS INDEX
BMI percentiles

WAIST CIRCU MFERE NCE

ASSESSMENT OF OBESITY

BMI = BODY MASS INDEX = weight (kg)/height^2 (m^2)

BMI percentiles - children

WAIST CIRCUMFERENCE

- **indicator of intraambdominal adipose mass**
- **predictor of cardio-metabolic risk**
- **↓ *sensitivity and specificity compare to EAT***

EPICARDIAL ADIPOSE TISSUE (EAT)

?

EPICARDIAL ADIPOSE TISSUE

- ***Visceral fat deposit located between the heart and the pericardium***
- ***Correlation with traditional cardio-metabolic RF***
- **Potential association with CAD and atherosclerosis (subclinical)**



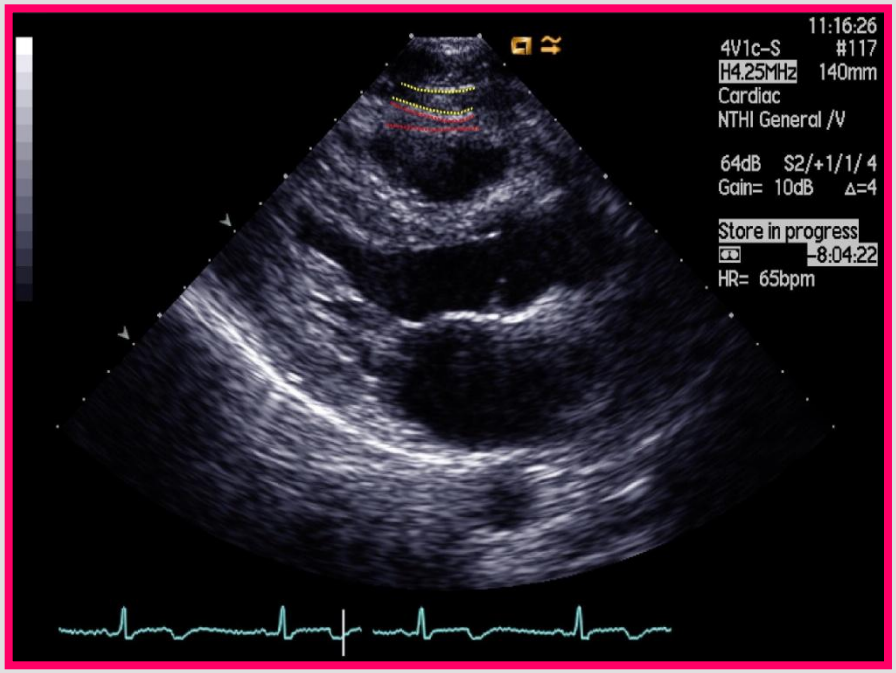
DOUBLE ROLE:

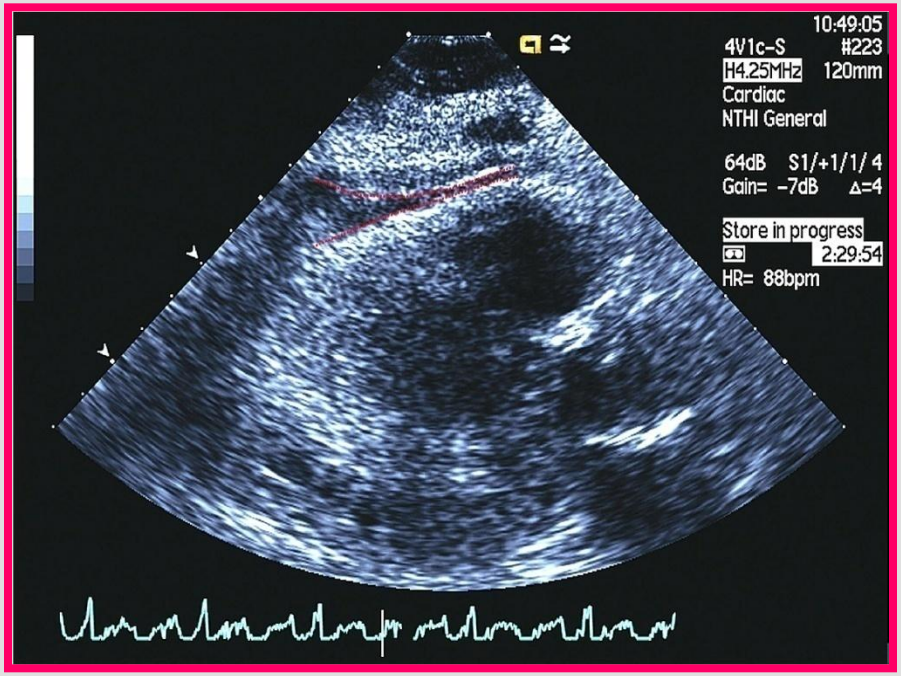
- ***Unfavorable:*** ***proinflammatory and proatherogenic cytokines*** **(TNF-α, monocyte chemoattractant protein–1, interleukin-6, rezistin, visfatin, omentin, leptin...)**
- ***Protective*****: antiinflamatory and antiatherogenic adipokines (adiponectin and adrenomedulin)**

Iacobellis a Pistilli a spol., 2005; Iacobellis a Barbaro a spol., 2008; Natale a spol. 2009, Iacobellis a Pellicelli a spol., 2007

EAT THICKNESS

- ❖ Expression of the visceral adipose tissue quantity
- ❖ Independent predictor of visceral adiposity
- ❖ Echocardiographic measurement → correlation with MRI measurement

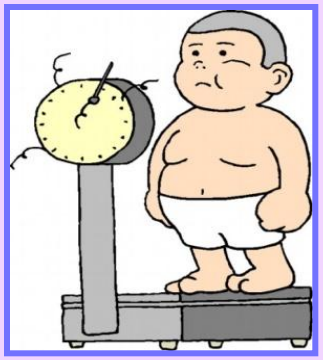




Iacobellis G et al., *Obes Res*. 2003;11:304–10. Abaci A,. Et al., *Int J Obes*. 2009; Schusterova, I. et al., *Pediatric Obesity*, 2012.



EAT, WC, BMI correlations



ADULTS

- EAT correlates with WC, BUT not with BMI
- EAT is ↑ with ↑ WC, BUT not with ↑ BMI

CHILDREN

- EAT correlates with WC and with BMI
- WC does not correlate better than BMI with CV RF → BMI and WC → similar predictive value of MS

Iacobellis G., Willens H.J.,*Obesity* (Silver Spring). 2008; Zimmet P, et al., *Pediatr Diabetes*. 2007; Iacobellis G., Leonetti F., *Clin Cardiol.* 2003; Ozdemir O. et al., *J Pediatr.* 2010



EAT and MS and IR and NAFLD



Adults

- ❑ ***Confirmed correlations***
- **EAT with IR**
- **EAT with MS**
- **EAT with AST and ALT (NAFLD markers)**

Children

- ❑ ***Not confirmed yet***
- **EAT and MS and IR**
- ❑ **Not clarified enough**
- **EAT and NAFLD**

Pellicelli A.M.,*Obesity (Silver Spring). 2008;* Iacobellis G, Willens H.J., *Obesity (Silver Spring). 2008;* Fernández J.R. et al., *J Pediatr. 2004;* Iacobellis G., Leonetti F. *J Clin Endocrinol Metab. 2005;* Barzin M, et al., *Acta Paediatr. 2011;* Abaci A,. At al.: *Int J Obes. 2009;* Mazur A. et al.: *Atherosclerosis. 2010*

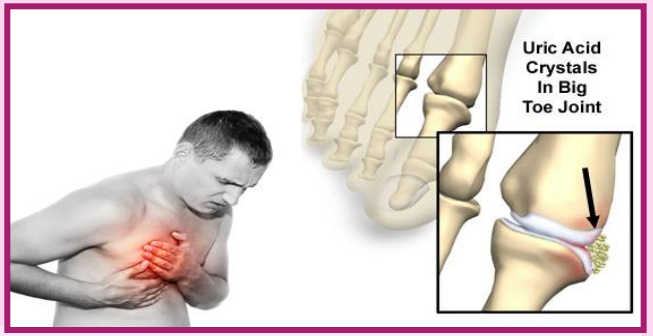
NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)



- **Fat accumulation in the liver**
- **Associated with obesity**
- **Hepatocytes damage and destruction → IR a ↑ production of proinflammatory cytokines, oxidative stress and mitochondrial dysfunction**
- **↑ mortality of patients with NAFLD compare to other population**

Barzin M. et al. : *Acta Paediatr.* 2011; Schmidt M. D. et al.: *Int J Obes* (Lond). 2011 ; Iacobellis G. et al.: *J Am Soc Echocardiogr.* 2009; Iacobellis G. *Nat Rev Endocrinol.* 2015

URIC ACID (UA)



- **UA independent CV RF → NHANES I study (National Health and Nutrition Survey)**
- **UA → negatively affect the development and progression of CVD by *stimulating inflammatory responses***
- **Framingham Heart Study → CV risk ↑ with ↑ UA in asymptomatic adults in all age**
- **Hyperuricemia → related to body fat accumulation (confirmed correlation between UA and visceral adiposity in adults)**

Zimmet P. et al.: *Lancet*. 2007; Fu J. F. et al.: *World J Gastroen-terol*. 2011; Fang J. et al. The NHANES I epidemiologic follow-up study, *JAMA*. 2000; Culleton B.F., et al.: The Framingham Heart Study. *Ann Intern Med*. 1999, Borghi, C. et al., *Expert Rev Cardiovasc Ther*. 2014

OUR STUDY







AIM OF OUR STUDY

Echocardiographic assessment of EAT thickness and its association with cardio-metabolic risk factors in overweight and obese children



STUDY GROUPS AND METHODS

In 25 (mean age 13.0 ±2.3) overweight and obese subjects and 24 lean controls, blood pressure (BP), waist circumference (WC), fasting plasma glucose and insulin, lipids, uric acid (UA), and hepatic enzymes were measured. EAT thickness was measured by transthoracic echocardiography



RESULTS

The anthropometric and clinical characteristics of the study and control group

Variables	Overweight and obese	Normal body weight	p-value
Body weight (kg)	72.3 ± 19.6	50.5 ± 14.3	$p < 0.01$
BMI (kg/m^2)	27.4 ± 3.5	18.8 ± 3.1	$p < 0.01$
BMI percentile	94.3 ± 3.5	36.2 ± 2.83	$p < 0.01$
BMI Z-score	-0.38 ±1.014	2.09 ± 0.51	$p < 0.01$
Systolic BP (mmHg)	133.4 ± 16.4	120.3 ± 17.4	$p < 0.05$
Diastolic BP (mmHg)	80.3 ± 11.5	69.7 ± 7.4	$p < 0.01$
Waist circumference (cm)	95.5 ± 12.6	73.1 ± 8.8	$p < 0.01$

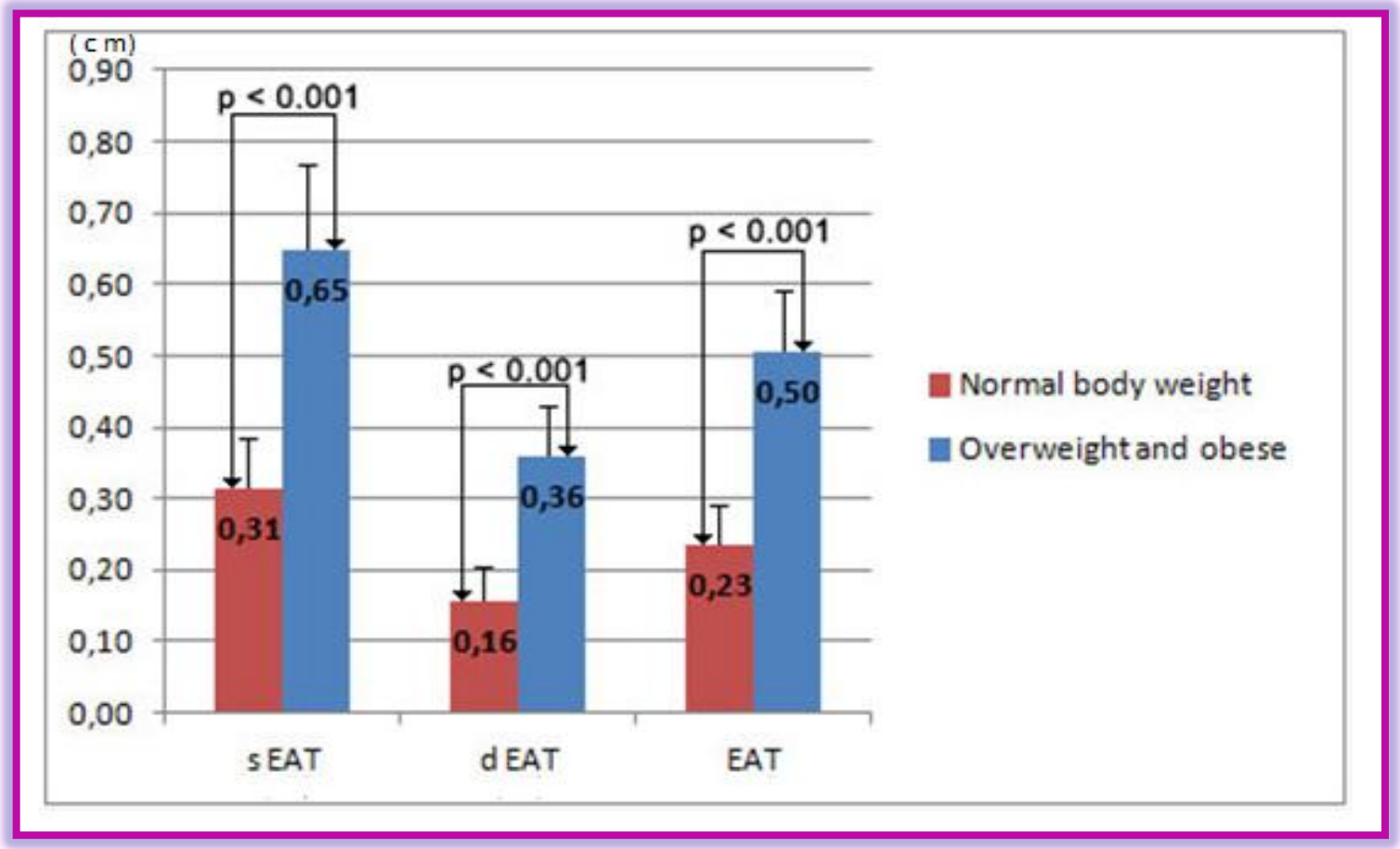
Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

The biochemical characteristics of the study and control group

Variables	Overweight and obese	Normal body weight	p-value
Fasting insulin	15.35 ± 7.2	8.01 ± 4.2	p < 0.05
Total cholesterol (mmol/l)	5.2 ± 1.2	4.2 ± 0.	p < 0.05
Triglyceride (mmol/l)	1.9 ± 1.1	0.7 ± 0.3	p < 0.01
HDL cholesterol (mmol/l)	1.2 ± 0.2	1.5 ± 0.2	p < 0.05
LDL cholesterol (mmol/l)	3.1 ± 1.2	2.4 ± 0.7	p < 0.05
Total Proteins (g/l)	75.9 ± 4.5	72.8 ± 3.6	p < 0.05
ALT (U/l)	42 ± 30	18 ± 6	p < 0.01
γGT (U/l)	30 ± 18	18 ± 6	p < 0.05
ApoB (g/l)	0.9 ± 0.3	0.6 ± 0.2	p < 0.01
HOMA index	3.47 ± 1.97	1.9 ± 1.68	P < 0.01

Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

EPICARDIAL ADIPOSE TISSUE (EAT) THICKNESS mean value



Schusterova , I. et al.: Circulation, 125:e741-e925; 2012;

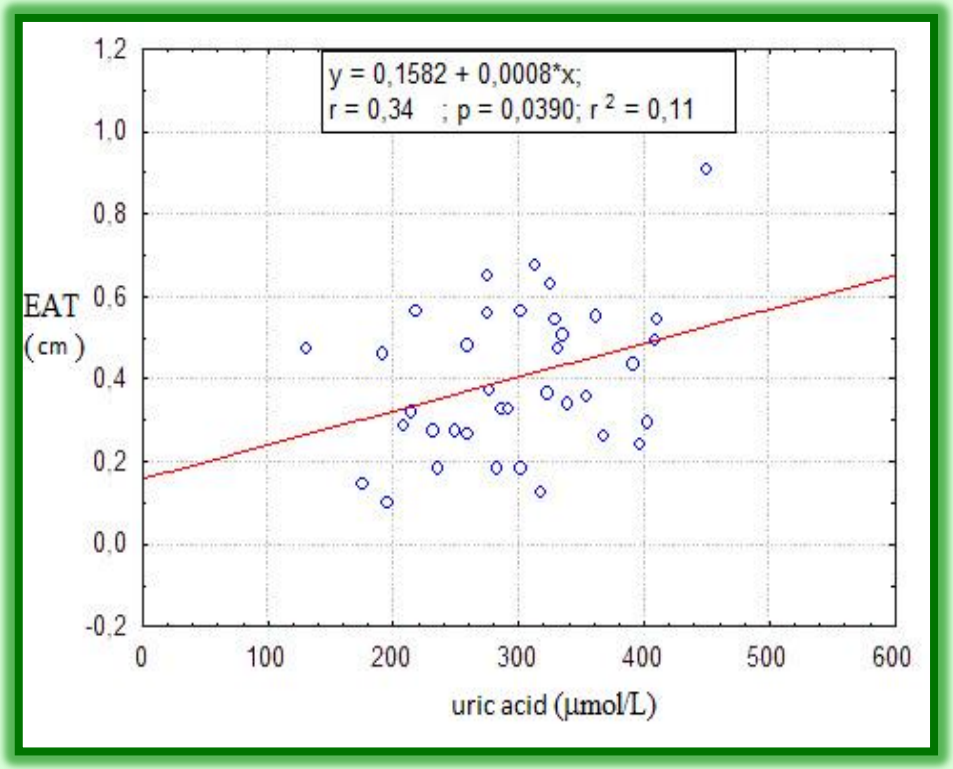
EAT correlations with clinical and biochemical parameters

Variable	Mean EAT	
	r	p-value
Body weight (kg)	0.63	p<0.0001
BMI – (kg/m^2)	0.80	p<0.0001
BMI percentile	0.72	p<0.0001
Waist circumference (cm)	0.68	p<0.0001
Systolic BP (mmHg)	0.40	p<0.05
Diastolic BP (mmHg)	0.43	p<0.01
Triglyceride [mmol/l]	0.68	p<0.0001
HDL cholesterol (mmol/l)	-0.50	p<0.001
Total proteins (g/l)	0.37	p<0.05
ApoB (g/l)	0.37	p < 0.05
Uric acid (umol/l)	???	
ALT (U/l)	???	

Schusterova I. et al.: JAHA, 4, 2012;

NEW FINDINGS OF CURRENT STUDY I.

Confirmed relationship between hyperuricaemia and epicardial fat



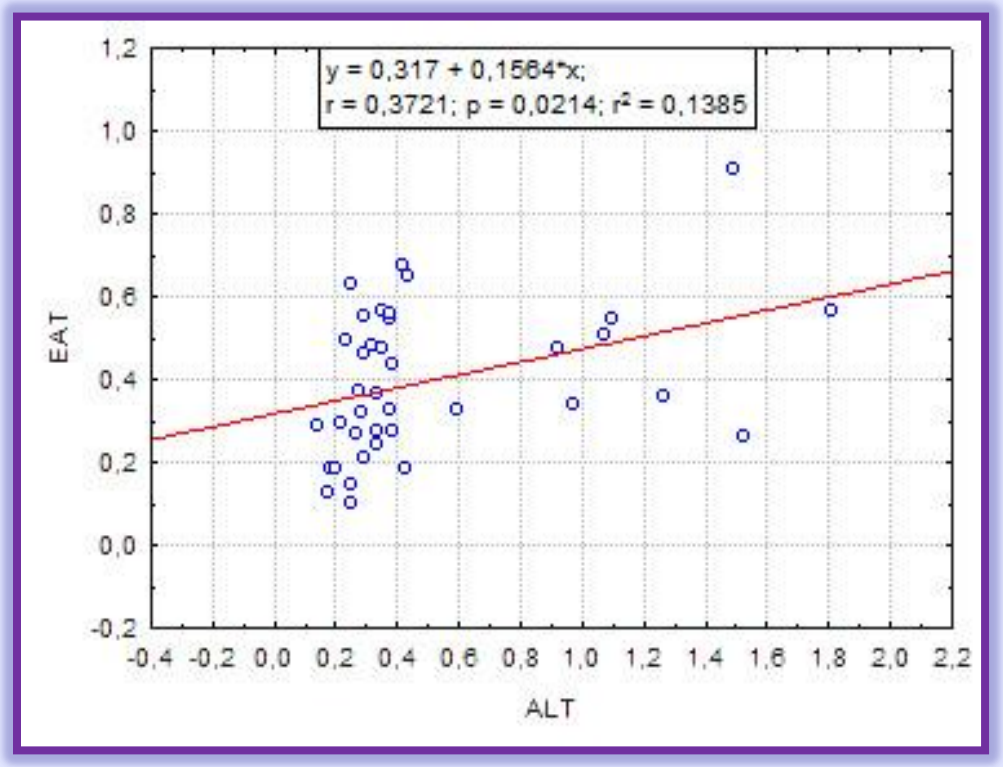
Variable	Overweight and obese	Normal body weight	p-value
Uric acid (umol/l)	321.4 ± 67.5	281.9 ± 69.3	0.16

Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

NEW FINDINGS OF CURRENT STUDY II.

Variable	Mean EAT	
	r	p-value
AST (U/l)	0.29	0.15
γGT (U/l)	0.31	0.06
ALT (U/l)	0.37	p<0.05

Confirmed relationship between epicardial fat, a marker of visceral adiposity and ALT, marker of NAFLD



Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

Multiple regression analysis of some metabolic variables

Variables	Mean EAT (cm)			
	r	tc	β coefficient	p value
Triglyceride [mmol/l]	0.732	**2.49**	**0.50**	**p < 0.05**
HDL cholesterol [mmol/l]		-1.04	-0.16	0.30
Urea acid [µmol/l]		0.79	0.11	0.43
Total proteins [g/l]		1,26	0.17	0.21
ALT [U/l]		0.44	0.06	0.66
ApoB [g/l]		-0.38	-0.06	0.70

After adjusting for BW, BMI, BMI percentile, WC and systolic and diastolic BP

Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

EAT AND MS a IR

Variables	Overweight and obese	Normal body weight	p-value
Fasting insulin	15.35 ± 7.2	8.01 ± 4.2	p < 0.05
Fasting glucose (mg/dL)	89.45± 9.1	88.67 ± 8.2	0.42
HOMA index	3.47 ± 1.97	1.9 ± 1.68	P < 0.01

EAT and insulin resistance		
HOMA index ≥ 3.16	0.49 ± 0,11	p = 0.27
HOMA index < 3.16	0.46 ± 0.12	

Diastolic EAT and MS		
MS yes	0.39 ± 0.18	p = 0.34
MS no	0.34 ± 0.13	

EAT **0.41** mm → predictive value of IR in children
EAT **0.39** mm → 95. percentile

Abaci, A. Int J Obes 2009; Mazur A. et al.: Atherosclerosis. 2010;

Schusterova, I. et al., *Pediatric Obesity,* Vol. 9, no. 1, p. 63-70. 2014

Indicators of obesity and metabolic risk

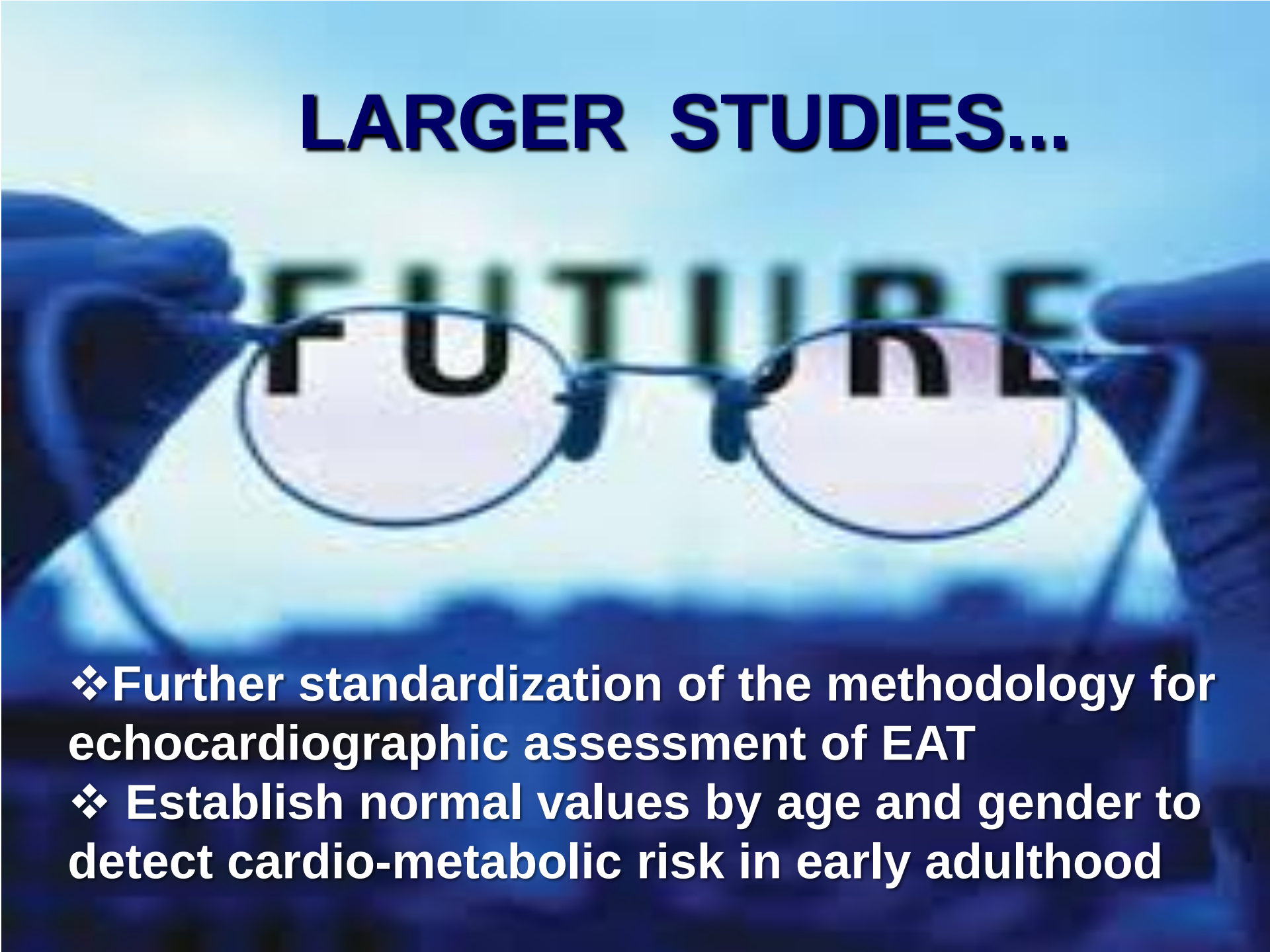
Variable	BMI (kg/m^2)		Mean EAT (cm)		WC (cm)	
	r	p-value	r	p-value	r	p-value
Systolic BP [mmHg]	0.58	p<0.001	0.40	p< 0.05	0.43	p< 0.05
Diastolic BP [mmHg]	0.63	p<0.001	0.43	p< 0.01	0.65	p<0.001
Triglyceride [mmol/l]	0.63	p<0.001	0.68	p<0.001	0.51	p< 0.01
HDL cholesterol mmol/l]	-0.49	p< 0.01	-0.50	p<0.001	-0.18	0.36
ApoB [g/l]	0.33	p< 0.05	0.37	p< 0.05	0.14	0.49
Uric acid [µmol/l]	0.41	p< 0.05	0.34	p< 0.05	0.37	0.06
Total proteins [g/l]	0.36	p< 0.05	0.37	p< 0.05	0.36	0.07
ALT [U/l]	0.51	p< 0.01	0.37	p< 0.05	0.38	0.06
γGT [U/l]	0.52	p<0.001	0.31	0.08	0.34	0.10

Metabolic risk assessment → **PREDICTORS**
BMI > EAT > WC

IN CONCLUSION...

- **Echocardiographic measurement of EAT is an easy and reliable method for assessing true visceral adiposity**
- **The extent of EAT could identifies children with an unfavorable cardio-metabolic risk profile including biochemical signs of NAFLD and hyperuricemia**
- **EAT is a better predictor than WC, however, BMI and EAT have a similar predictive value for assessment of metabolic impairment**
- It is not clear whether the extent of visceral adipose tissue is also predictive for IR in pediatric patients

LARGER STUDIES...



- Further standardization of the methodology for echocardiographic assessment of EAT
- Establish normal values by age and gender to detect cardio-metabolic risk in early adulthood


Thank you for your attention !
KOSICE, SLOVAKIA - WINTER