ORIGINAL ARTICLE

Definition of new cut-offs of BMI and waist circumference based on body composition and insulin resistance: differences between children, adolescents and adults

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Received 11 April 2017; revised 7 June 2017; accepted 21 June 2017

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Summary

Objective

This study aims to determine associations between anthropometric traits, regional fat depots and insulin resistance in children, adolescents and adults to define new cut-offs of body mass index (BMI) or waist circumference (WC).

Design

Cross-sectional data were assessed in 433 children, adolescents and adults (aged: 6–60 years, BMI: 23.6 [21.0–27.7] kg m^{-2}). Total adipose tissue (TAT), regional subcutaneous adipose tissue (SAT_{total}, SAT_{trunk}) and visceral adipose tissue (VAT) were determined by whole-body magnetic resonance imaging, fat mass by air-displacement plethysmography. Insulin resistance was evaluated by homeostasis model assessment of insulin resistance (HOMA-IR). Bivariate as well as partial correlations and regression analyses were used. Cut-off values of BMI and WC related to regional fat depots and HOMA-IR were analysed by receiver operating characteristics curve.

Results

In adults, TAT, SAT_{total} and SAT_{trunk} increased linearly with increasing BMI and WC, whereas they followed a cubic function in children and adolescents with a steep increase at BMI and WC ≥1 standard deviation score and VAT at WC ≥2 standard deviation score. Sex differences were apparent in adults with women having higher masses of TAT and SAT and men having higher VAT. Using established BMI or WC cut-offs, correspondent masses of TAT, SAT_{total}, SAT_{trunk} and VAT increased from childhood to adulthood. In all age groups, there were positive associations between BMI, WC, SAT_{trunk}, VAT and HOMA-IR. When compared with normative cut-offs of BMI or WC, HOMA-IR-derived cut-offs of regional fat depots were lower in all age groups.

Conclusions

Associations between BMI, WC and regional fat depots varied between children, adolescents, young and older adults. When compared with BMI-derived and WC-derived values, an insulin resistance-derived cut-off corresponded to lower masses of regional fat depots. Thus, established BMI and WC cut-offs are not appropriate to assess metabolic disturbances associated with obesity; therefore, new cut-offs of BMI and WC are needed for clinical practice.

Keywords: body composition, body fat distribution, insulin resistance, obesity.

Introduction

Body mass index (BMI) and waist circumference (WC) are used to assess obesity and abdominal obesity in children, adolescents and adults (1,2). In epidemiological studies, these anthropometric traits are positively associated with cardiometabolic traits (3–6). However, anthropometric traits have considerable limitations. BMI can neither differentiate between fat mass (FM) and fat-free mass nor between regional fat depots (7–9). In addition, WC does not allow to distinguish between abdominal subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) (10). In daily practice, health-related cut-offs of BMI and WC are established in adult population (2). In children and adolescents, BMI and WC ≥97 age-specific and sex-specific percentiles are used as cut-offs (11,12). The cut-off data had been extrapolated to mortality risk in overweight and obese adults at BMI of 25 and 30 kg m^{-2} (13,14). These references are widely used in clinical and research practice. However, the associations between anthropometric traits and regional fat depots as well as insulin resistance have not been systematically addressed and may vary between children and adolescents compared with adults. Therefore, we questioned the statistical approach based on mortality risk estimates obtained in epidemiological studies.

To go beyond simple anthropometric traits, detailed body composition as assessed by whole-body magnetic resonance imaging (MRI) or computed tomography is used (9). The aims of this study were to determine associations between simple anthropometric traits and regional fat depots in children, adolescents and adults and to compare masses of regional fat depots at either BMI or WC or insulin resistance-derived cut-offs in different age and sex groups.

Methods

Subjects

This investigation was a secondary analysis. The study sample included pooled data of 433 healthy Caucasian subjects who participated in different studies at the 'Reference Center for Body Composition' (Institute of Human Nutrition and Food Science at the University of Kiel, Germany) between 2005 and 2016 as described in detail elsewhere (15–18). Cross-sectional data of 151 children and adolescents (aged: 6–18 years; BMI: 21.0 [18.0–27.6]), 150 young adults (aged: 18–30 years; BMI: 23.5 [22.0–26.7]) and 132 adults (aged: 30–60 years; BMI: 24.4 [22.8–28.5]) were analysed. The recruitment was conducted by local advertisements and notice board postings. Exclusion criteria were metallic implants, pregnancy, smoking, chronic or acute diseases and medication intake. Each participant underwent examinations of anthropometry and body composition at the Institute of Human Nutrition (University of Kiel, Germany). Whole-body MRI was performed at the Clinic for Diagnostic Radiology (University Medical Center Schleswig-Holstein, Kiel, Germany). Pubertal stage was self-assessed according to the definition of Marshall and Tanner (19). Breast and genital stages were used to categorize pubertal status into three groups (prepubertal: Tanner I; intrapubertal: Tanner II–III, postpubertal: Tanner ≥ IV) (20). Because of a low number of prepubertal children (n = 26), prepubertal and intrapubertal subjects were grouped together. Before participation, written informed consent was received from each participant and, in state of minority, from its legal guardian. All studies were authorized by the ethical committee of the University Kiel and conducted according to the guidelines laid down in the 'Declaration of Helsinki'.

Anthropometric measurements

Body weight was determined to the nearest 0.01 kg using a Tanita scale coupled to the BOD POD® Body Composition Tracking System (Life Measurement Instruments, Concord, California, USA) with subjects wearing underwear. Height was assessed without shoes to the nearest 0.5 cm by using a stadiometer (SECA, Modell 220, Hamburg, Germany). BMI was calculated as body weight (kg) / body height $(m)^2$. WC was measured with the subjects standing in upright position midway between the lowest rib and the top of the iliac crest. At the end of a normal expiration, the measurement was performed with a non-elastic plastic tape positioned parallel to the floor. BMI and WC values were converted to standard deviation score (SDS) values in children and adolescents using the lambda-mu-sigma (LMS) method from Cole (21). The calculation was based on German reference data for children and adolescents (11,12). Cut-offs for the definition of obesity and abdominal obesity in children and adolescents were BMI ≥ 2 SDS and WC ≥ 2 SDS (22). In adults, obesity was defined as BMI ≥ 30 kg m^{-2}, whereas cut-offs for abdominal obesity were WC > 88 cm in women and WC > 102 cm in men (23).

Densitometry

Air-displacement plethysmography was performed by BOD POD® device. In children and adolescents, specific equations were used to assess FM as in detail described elsewhere (24). The equation by Siri *et al.* was used to calculate FM in adults (25).

Magnetic resonance imaging

Detailed body composition was performed by using whole-body MRI with a 1.5T scanner (Magnetom Vision or Magnetom Avanto, Siemens Medical Systems, Erlangen, Germany) as in detail described elsewhere (26,27). Briefly, participants were examined in a supine position with their arms extended above their heads. SAT_{arms} were defined from wrist to humerus heads. SAT_{legs} were defined from femoral heads to ankle. Between humerus and femoral heads, volume of SAT_{trunk} was assessed. VAT was defined from the top of the liver to femoral heads. In the present analysis, volumes of SAT and VAT were manually segmented by using segmentation software (SliceOmatic 4.3 and 5.0, Tomovision, Montreal, Canada). Tissue volumes were determined from the sum of all areas (cm^2) multiplied by slice thickness. Masses of regional SAT and VAT were calculated as tissue volumes multiplied by density (0.923 g cm^{-3}).

Homeostasis model assessment of insulin resistance

Blood samples were taken after an 8-h overnight fast and analysed by standard procedures. Plasma glucose was determined enzymatically using Konelab-Test-Kit (Thermo Clinical Labsystems, Frankfurt, Germany). Plasma insulin was measured by radioimmunoassay (Adaltis, Freiburg, Germany). Homeostasis model assessment of insulin resistance (HOMA-IR) was used to determine insulin resistance:

HOMA-IR = plasma glucose (mmol L^{-1}) × plasma insulin (μU ml^{-1}) / 22.5 (28). Because there is no recommended threshold for insulin resistance in children, adolescents and adults, a cut-off of 2.5 was used to separate participants into having normal or elevated HOMA-IR (29,30).

Statistical analysis

All statistical analyses were carried out with SPSS statistical software (SPSS 24.0, Inc., Chicago, Illinois, USA). Data were given as median and interquartil range because of not normally distributed data. Mann–Whitney *U* test and Kruskal–Wallis test with bonferroni correction were used to assess differences between groups. To examine the association between BMI and FM, bivariate correlations were performed. Age-adjusted and gender-adjusted partial correlations were used to determine the association between anthropometric traits, regional fat depots and insulin resistance in children, adolescents and adults. Further, regression analyses were carried out to determine the associations between BMI, WC and regional fat depots in different age groups. Receiver operating characteristics curve analyses demonstrated the ability of regional fat depots to discriminate against elevated HOMA-IR. Further, Youden's index was used to obtain the optimal cut-off value for the detection of elevated HOMA-IR. Significance was set at $P < 0.05$ for all tests.

Results

The main characteristics of the study population are shown in Table 1. In both genders, BMI, WC, total adipose tissue (TAT), SAT_{trunk} and VAT were significantly higher in young adults when compared with children. When compared with male young adults, WC, FM, TAT and VAT were higher in male adults with no differences in women. In women, HOMA-IR was highest in young adults, whereas in men, HOMA-IR was highest in adolescents. In children, anthropometric traits and regional fat depots did not differ between men and women. By contrast, WC, FM, TAT, SAT_{total}, SAT_{trunk} and VAT differed significantly between female and male adults.

Association between body mass index and fat mass in children, adolescents and adults

Associations between BMI and FM in children, adolescents, young adults and adults are shown in Figure 1. These associations were strong in children and adolescents but moderate in young and older adults. The explained variance of FM by BMI was highest in children and decreased with increasing age. Sex differences in the BMI – FM – association became apparent in adolescents and were most obvious in adults. Sensitivity of BMI to predict FM was high in all age groups; by contrast, specificity decreased from children to adults.

Association between anthropometric traits and masses of regional fat depots

Associations between BMI, WC and regional fat depots in children, adolescents, young adults and adults are shown in Figure 2. In children and adolescents, associations between either BMI or WC and regional fat depots followed a cubic function. TAT, SAT_{total} and SAT_{trunk} were constant until about 1.0 SDS and started to increase beyond that number. VAT increased with WC > 2 SDS. In contrast to children and adolescents, the associations between either BMI or WC and regional fat depots were linear in young and older adults. TAT, SAT_{total}, SAT_{trunk} and VAT increased with increasing BMI or WC. Sex

Table 1 Characteristics of the study population stratified by age group and gender[1]

	Children		Adolescents		Young adults		Adults	
	Female	Male	Female	Male	Female	Male	Female	Male
BMI (kg/m^2)	19.3[2] (16.5–25.5)	19.0 (15.7–24.9)	21.8 (19.8–29.6)	23.4[3] (20.0–31.1)	23.9[3] (21.7–31.8)	23.4[3] (22.1–25.7)	24.3[3] (21.7–27.7)	24.5[3] (23.2–28.7)
WC (cm)	65.5 (57.5–83.8)	73.0 (58.0–87.5)	75.3[3] (68.8–99.5)	78.3 (72.5–99.0)	81.0[3] (74.0–96.8)	85.0[3] (81.0–89.0)	83.0[3] (77.5–94.0)	**89.5**[3,4,5] (84.0–99.0)
FM (%)	22.6 (16.1–36.3)	20.1 (15.5–27.1)	25.9 (23.0–39.5)	**20.2** (14.6–31.2)	32.0[3] (27.9–43.4)	**16.5** (13.2–22.9)	34.3[3] (28.4–41.6)	**22.1**[5] (16.5–27.9)
TAT (kg)	9.5 (7.1–19.3)	9.0 (4.7–18.5)	15.0 (11.9–29.1)	11.6 (8.4–25.0)	21.5[3] (17.5–34.6)	**12.9**[3] (10.8–18.6)	22.6[3] (17.0–30.8)	**18.2**[3,5] (14.0–24.5)
SAT$_{total}$ (kg)	9.1 (6.9–18.8)	8.7 (4.6–17.9)	14.5 (11.5–27.9)	**11.3** (8.1–23.2)	20.0[3] (17.0–33.3)	**11.8** (10.2–17.2)	21.4[3] (16.1–28.3)	**14.8**[3] (11.7–18.6)
SAT$_{trunk}$ (kg)	2.9 (2.1–6.3)	2.6 (1.3–6.7)	4.7 (3.7–13.5)	3.8 (2.8–10.4)	8.6[3] (6.2–14.3)	**4.7**[3] (3.7–8.1)	9.1[3] (6.3–13.3)	**6.8**[3] (4.9–9.0)
VAT (kg)	0.36 (0.22–0.87)	0.29 (0.16–0.88)	0.47 (0.34–0.96)	0.64 (0.37–1.30)	1.1[3,4] (0.6–1.7)	1.1[3] (0.7–2.1)	1.4[3,4] (0.7–2.3)	**2.5**[3,4,5] (1.7–5.2)
HOMA-IR	1.9 (1.0–2.4)	1.8 (0.9–2.8)	2.5 (1.5–3.1)	2.3 (1.5–3.1)	2.7[3] (1.6–4.3)	**1.6** (1.2–2.1)	2.2 (1.5–2.8)	2.0 (1.4–3.3)

[1]BMI, body mass index; FM, fat mass; HOMA-IR, homeostasis model assessment of insulin resistance; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.
[2]Median (IQR) (all such values).
Median in bold, significantly different from women (Mann-Whitney *U* test, $P < 0.05$).
[3]Significantly different from children for either women or men;
[4]significantly different from adolescents for either women or men;
[5]significantly different from young adults for either women or men (Kruskal–Wallis test with Bonferroni correction, $P < 0.05$).

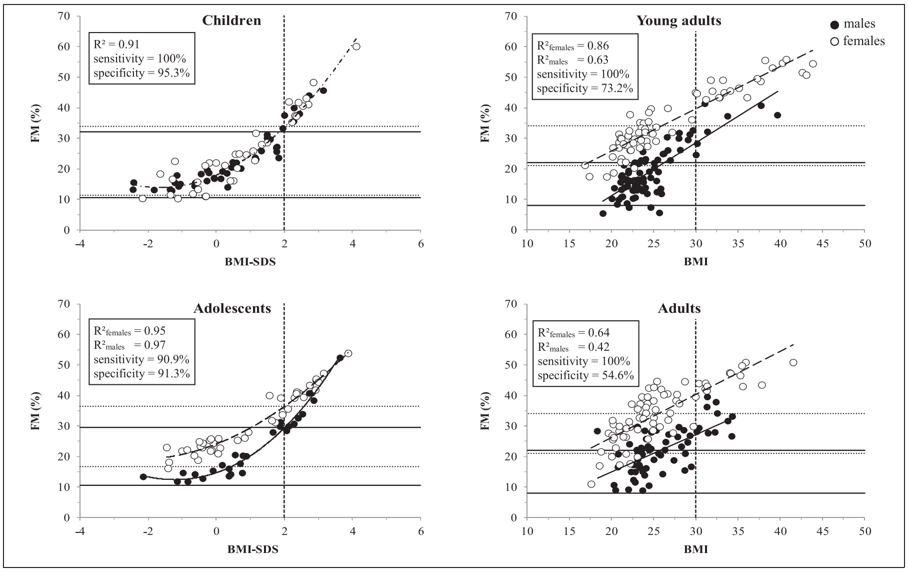

Figure 1 Association between BMI and fat mass (%) in children, adolescents, young adults and adults stratified by gender. Cut-offs of body mass index (BMI) and BMI standard deviation score (SDS) are presented as vertical dashed lines (11,12). Range of normal fat mass (%) is presented as horizontal dashed (females) and solid (males) lines (35,36). Abbreviation: FM, fat mass.

differences became apparent in adolescents and were most obvious in adults with women having higher masses of TAT, SAT_{total} and SAT_{trunk} and men having higher masses of VAT.

The explained variance of all regional fat depots by BMI-SDS and WC-SDS was high in children and adolescents. It decreased in young and older adults. When compared with men in young and older adults, the explained variance of TAT, SAT_{total} and SAT_{trunk} by BMI and WC was higher in women.

The cut-offs of 2.0 SDS in BMI and WC were appropriate to discriminate higher masses of regional fat depots in children and adolescents. In adults, WC cut-offs were less appropriate to discriminate higher masses of regional fat depots.

TAT, SAT_{total}, SAT_{trunk} and VAT at either elevated BMI or WC differed between age and sex groups (Table 2). The corresponding regional fat depots increased from childhood to adulthood. Further, in adolescents and adults, masses of TAT, SAT_{total} and SAT_{trunk} were higher in women with men having higher masses of VAT.

Association between anthropometric traits and masses of regional fat depots with homeostasis model assessment of insulin resistance

Associations between either anthropometric traits or regional fat depots and HOMA-IR in children, adolescents, young adults and adults are shown in Figure 3. In all age groups, moderate and positive associations were found between either BMI or WC or SAT_{trunk} or VAT and insulin resistance. Accordingly, sex differences were minor. When compared with anthropometric traits and SAT_{trunk}, highest correlations were seen between VAT and insulin resistance with no differences between the different age groups.

Using a HOMA-IR of 2.5 as a cut-off, the corresponding masses of regional fat depots varied between the different age groups (Table 2). Comparing the corresponding masses of TAT, SAT_{total}, SAT_{trunk} and VAT derived from either normative anthropometric traits or HOMA-IR, cut-offs showed lower masses for the latter calculation. These cut-offs are demonstrated as horizontal lines in Figure 2. Each gender-dependent vertical arrow marked the corresponding BMI or WC value. An insulin resistance-derived classification led to lower BMI or WC cut-offs for elevated disease risk.

Discussion

In adults TAT, SAT_{total}, SAT_{trunk} and VAT increased linearly with increasing BMI and WC. When compared with adults, the associations followed a cubic function in children and adolescents. There was a sex difference: Women had higher masses of TAT and SAT with men having higher VAT. Using established BMI or WC cut-offs, TAT, SAT_{total}, SAT_{trunk} and VAT increased from childhood

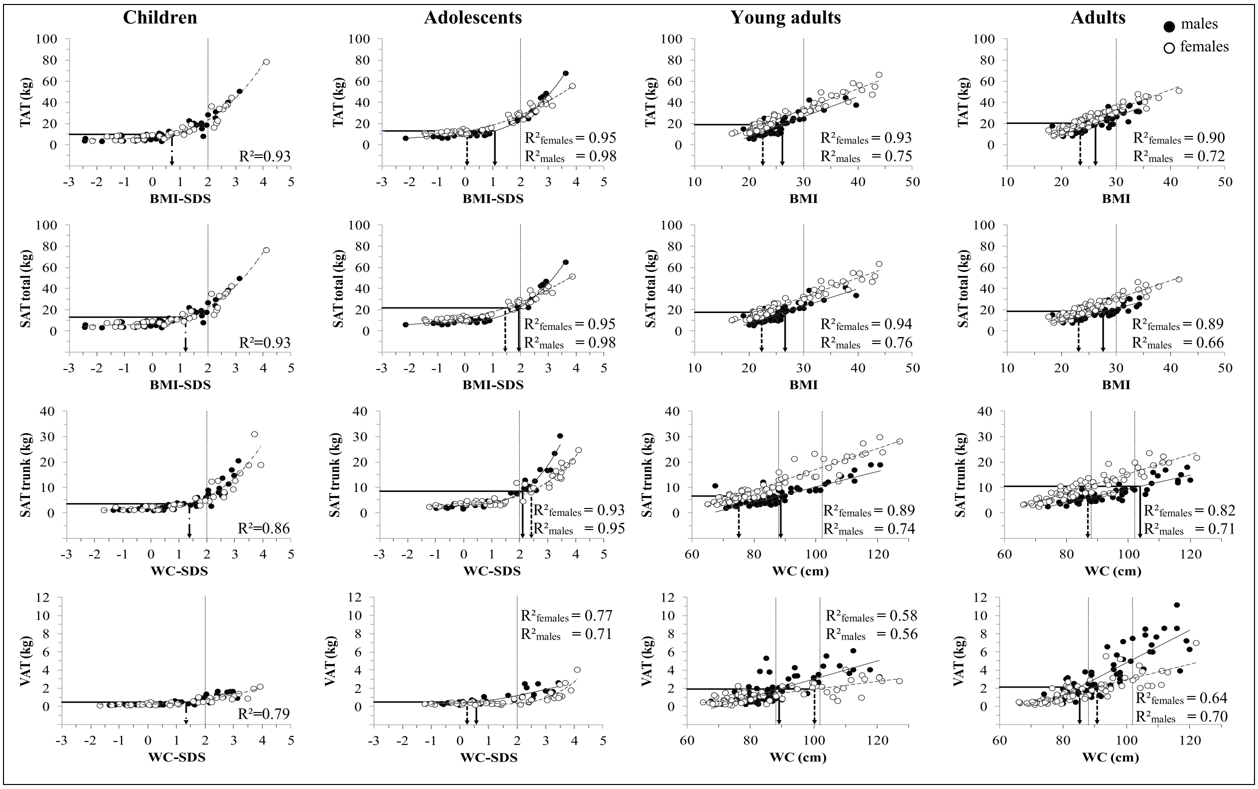

Figure 2 Association between anthropometric traits and regional fat depots in children, adolescents, young adults and adults stratified by gender. Cut-offs of body mass index standard deviation score (BMI-SDS), BMI, waist circumference (WC)-SDS and WC are presented as vertical dashed lines. Cut-offs based on receiver operating characteristics (ROC) curve analyses (Table 2) for predicting elevated homeostasis model assessment of insulin resistance (HOMA-IR) (>2.5) are presented as horizontal solid lines. Accordingly, dashed/dotted (total children), dashed (females) and solid (males) arrows marked the corresponding BMI-SDS, BMI, WC-SDS or WC values. Abbreviations: SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue.

to adulthood. When compared with the normative cut-offs of BMI or WC, insulin resistance-derived cut-offs of regional fat depots were lower in all age groups. To our knowledge, the current study is first to systematically investigate associations between BMI and WC vs. TAT, SAT_{total}, SAT_{trunk} and VAT by age group and gender as well as to compare masses of regional fat depots at either BMI or WC or insulin resistance derived cut-offs in a greater population of subjects aged 6 to 60 years.

Table 2 Cut-offs of regional fat depots on elevated HOMA, BMI and WC in children, adolescents, young adults and adults[1]

	Children[2]		Adolescents[2]		Young adults[2]		Adults[2]	
	HOMA-IR	BMI or WC	HOMA-IR	BMI or WC	HOMA-IR	BMI or WC	HOMA-IR	BMI or WC
TAT (kg)	9.8	23.3/23.1[3]	12.9	23.9/27.9	19.0	26.4/33.4	20.3	27.0/32.9
SAT total (kg)	12.8	22.3/22.2	21.6	22.7/27.1	17.7	23.4/31.8	18.4	21.4/30.3
SAT trunk (kg)	3.6	5.7/6.1	8.5	7.7/6.7	6.7	10.8/12.0	10.5	10.0/10.9
VAT (kg)	0.5	0.8/0.6	0.5	1.2/0.3	1.9	3.2/1.4	2.1	5.1/1.9

[1]BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance; SAT, subcutaneous adipose tissue; SDS, standard deviation score; TAT, total adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.

[2]Masses of regional fat depots based on elevated HOMA-IR, BMI (in children and adolescents BMI-SDS) or WC (in children and adolescents WC-SDS).

[3]Male regional fat mass/female regional fat mass (all such values).

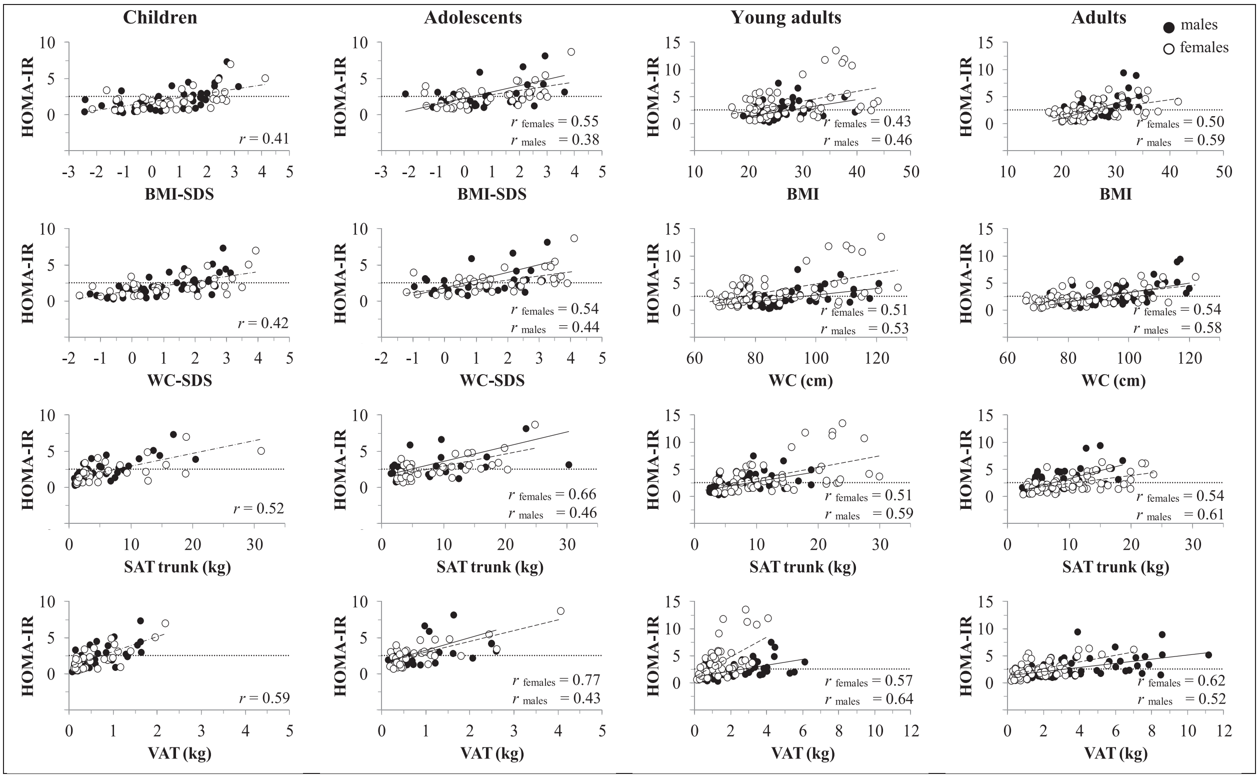

Figure 3 Association between anthropometric traits, regional fat depots and homeostasis model assessment of insulin resistance (HOMA-IR) in children, adolescents, young adults and adults stratified by gender. Cut-off of elevated HOMA-IR (>2.5), which is used in receiver operating characteristics curve analyses, is presented as horizontal dashed lines. All correlations were significant at $P < 0.05$. Abbreviations: SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.

In children and adolescents, FM, TAT, SAT and VAT followed a cubic function with a steep increase at BMI and WC $\geq$ 1 SDS (Figure 2). This is contrary to previous studies showing linear relationships between anthropometric traits and regional fat depots in adolescents (10,31,32) whereas VAT increased exponentially with increasing BMI Z-Score or WC (33). The latter data are in line with our results. However, to our knowledge, the cubic association between anthropometric traits and either TAT or SAT_{total} or SAT_{trunk} or VAT has not been previously shown in children and adolescents. Our results indicated that in children and adolescents, masses of regional fat depots started to increase beyond a BMI and WC $\geq$ 1 SDS only. Contrary to children and adolescents, in young and older adults, masses of regional fat depots increased linearly with increasing anthropometric traits with women having higher masses of TAT, SAT_{total} and SAT_{trunk} and men having higher masses of VAT. These data confirm with previous findings in adults (9,18,34,35).

The corresponding masses of TAT, SAT_{total}, SAT_{trunk} and VAT using BMI and WC cut-offs differed between age and sex groups and increased from childhood to adulthood (Table 2). These findings indicated that BMI and WC cut-offs inadequately describe masses of regional fat depots in different age and sex groups. In addition, insulin resistance-derived cut-offs of regional fat depots varied between age groups and also increased from childhood to adulthood. Comparing cut-offs of masses of individual fat depots derived from anthropometric traits and HOMA-IR gave considerably lower values for the latter calculation (Figure 2, Table 2). The data showed only moderate associations between measures of body fat and insulin resistance. Our findings suggested that insulin resistance (as reflected by biomarkers, i.e. HOMA-IR) is not primarily determined by masses of fat depots. In line with our results, previous cross-sectional data also showed only moderate associations between regional fat depots and insulin resistance in children, adolescents and adults (10,36,37). When compared with BMI, recent studies have shown that FM adjusted for height improved the prediction of insulin resistance in adults with no improvements in children and adolescents (38–42). However, insulin resistance results from a multidimensional dynamic process, which cannot be addressed in a cross-sectional study. Therefore, longitudinal data from birth to adulthood would be conducive. In addition, other determinants of insulin resistance are important to be considered: Adipose tissue remodelling is altered by hyperplasia and or hypertrophy (43). Studies have shown that hypertrophy led to increased secretion of pro-inflammatory cytokines, which were supposed to result in the development of insulin resistance (44–46). Accordingly, most data on hypertrophy and its association to insulin resistance in humans were obtained in obese subjects undergoing bariatric surgery (47,48). A final argument is that HOMA-IR most probably reflects hepatic insulin resistance (49). By contrast, the euglycemic clamp technique, which is considered as the present gold standard in the assessment of insulin sensitivity, measures the stimulation of peripheral, i.e. skeletal muscle glucose uptake (50). Based on our data, we found a correlation of $r = -0.67$ between euglycemic clamp technique and HOMA-IR (51,52). Therefore, the association between FM and insulin sensitivity also depends on the methods used to assess insulin resistance.

To our knowledge, this is the first study to systematically investigate associations between anthropometric traits and regional fat depots in children, adolescents and adults and to compare masses of regional fat depots at either BMI or WC or insulin resistance-derived cut-offs. Regional fat depots were measured by whole-body MRI. This is the gold-standard method of body composition. In addition, metabolically derived cut-offs were chosen to compare the corresponding masses of regional fat depots in different age groups. A limitation of this study is that we have analysed prepubertal and intrapubertal subjects together because of the small number of prepubertal children. Thus, no further differentiation can be performed in this age group. In addition, the associations of HOMA-IR by anthropometric traits and regional fat depots were only moderate. Additional data on muscle mass and ectopic lipids in muscle and liver may add to improve these associations.

Associations between simple anthropometric traits and regional fat depots differed between children and adolescents vs. young and older adults. When compared with the established BMI or WC cut-offs, corresponding masses of regional fat depots varied between age groups and gender. There were positive associations between anthropometric traits and regional fat depots with HOMA-IR. Insulin resistance-derived cut-offs of regional fat depots were lower than the corresponding values based on normative BMI and WC cut-offs. This knowledge may contribute to a better evaluation of nutritional status based on health outcomes instead of normative cut-offs. Our results indicated that using established BMI or WC cut-offs in children, adolescents and adults partly fails to detect subjects with an elevated risk of insulin resistance. Thus, there is need for new cut-offs of BMI and WC for clinical practice. Because obesity is defined as an excessive fat accumulation, which impairs health (53), thus, in future, BMI and WC should be replaced by measures of body fat and regional fat depots taking into account their associations with metabolic disturbances.

Conflict of Interest Statement

The authors declared no conflict of interest.

Acknowledgements

We thank Britta Jux and the Clinic for Diagnostic Radiology, University Medical Center Schleswig-Holstein, Kiel (Germany), for the help with MRI scanning. We acknowledge financial support by Land Schleswig-Holstein within the funding programme Open Access Publikationsfonds.

Funding

Our own research data presented here have been funded by generous grants from the Federal Ministry of Education and Research (BMBF 01EA1336, 01GI1121A, 01GI1125, 01GI0821), the German Research Foundation (DFG Mü 714/8-3; DFG Bo 3296/1-1) and OMRON, Kyoto, Japan.

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