International Journal of Obesity (2006) 30, 23–30

0307-0565/06 $30.00
www.nature.com/ijo

PEDIATRIC HIGHLIGHT

Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children

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Background: The study of the relationship between anthropometry and visceral adipose tissue (VAT) is of great interest because VAT is associated with many risk factors for noncommunicable diseases and anthropometry is easy to perform in clinical practice. The studies hitherto available for children have, however, been performed on small sample sizes.
Design: Pooling of the data of studies published from 1992 to 2004 as indexed on Medline.
Aims: To assess the relationship between anthropometry and VAT and subcutaneous adipose tissue (SAT) as measured by magnetic resonance imaging (MRI) in children and to analyze the effect of age, gender, pubertal status and ethnicity.
Subjects and methods: Eligible subjects were 7–16 year-old, with availability of VAT and SAT, gender, ethnicity, body mass index (BMI) and waist circumference (WC). A total of 497 subjects were collected from seven different investigators and 407 of them (178 Caucasians and 229 Hispanics) were analyzed.
Results: Despite ethnic differences in MRI data, BMI, WC and age, no difference in VAT was found between Caucasians and Hispanics after correction for SAT and BMI. Univariate regression analysis identified WC as the best single predictor of VAT (64.8% of variance) and BMI of SAT (88.9% of variance). The contribution of ethnicity and gender to the unexplained variance of the VAT–WC relationship was low ($\leqslant$3%) but significant ($P\leqslant0.002$). The different laboratories explained a low ($\leqslant$4.8%) but significant ($P<0.0001$) portion of the unexplained variance of the VAT–WC and SAT–BMI relationships. Prediction equations for VAT (VAT (cm^2) = 1.1 × WC (cm)−52.9) and SAT (SAT (cm^2) = 23.2 × BMI (kg/m^2)−329) were developed on a randomly chosen half of the population and crossvalidated in the remaining half. The pure error of the estimate was 13 cm^2 for VAT and 57 cm^2 for SAT.
Conclusions: WC can be considered a good predictor of VAT as well as BMI of SAT. The importance of ethnicity and gender on VAT estimation is not negligible.
International Journal of Obesity (2006) **30,** 23–30. doi:10.1038/sj.ijo.0803163

Keywords: childhood obesity; magnetic resonance imaging; visceral adipose tissue; subcutaneous adipose tissue; waist circumference; body mass index

Introduction

The growing prevalence of childhood obesity[1–5] highlights two major problems for health professionals: (1) the identification and adoption of population-based prevention strategies involving healthy lifestyle beginning early in life, and, (2) the need to identify high risk obese children for targeted interventions. There is some agreement, especially in adults, that the assessment of fat distribution (visceral fat in particular), may be a useful approach for determining risk

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Received 27 February 2005; revised 20 September 2005; accepted 22 September 2005

of disease associated with obesity.[6–10] Since 1992, visceral adiposity has been evaluated by Magnetic Resonance Imaging (MRI) in children and it has been related to glucose metabolism, lipids abnormalities and hypertension.[11–20] However, direct measurements of visceral adipose tissue (VAT) cannot be proposed for field studies due to their cost and technical difficulties.[21] Several anthropometric indexes have been suggested as indexes of VAT. In adults, waist circumference (WC) is widely used as a surrogate of central fat distribution,[22] but in children it may be influenced by growth and puberty, reducing its accuracy in estimating VAT. Moreover, other variables, such as gender and ethnicity, may be important confounding factors.[23]

Recently, the relationship between anthropometry and metabolic risk factors has been examined and waist cutoffs suitable for clinical evaluation have been proposed in children and adolescents.[9,24–28] However, these studies did not measure VAT directly. The few available studies on VAT and anthropometry measurements in children were performed in small groups.[7,11–18,20] Therefore, the aims of our study were: (1) to pool data from various investigators to evaluate the relationship between anthropometry and MRI-derived abdominal fat in children, and, (2) to evaluate the effect of puberty and ethnicity on the relationship between anthropometry and MRI-derived abdominal fat.

Subjects and methods

In January 2004, a Medline-based search was performed to identify published studies on MRI in obese children since 1992. Lead authors of the identified studies were contacted and were invited to submit data for a pooled analysis. The following variables were collected: adipose tissue measured from MRI at lumbar L4 level (VAT area and subcutaneous adipose tissue (SAT) area), age, gender, ethnicity, pubertal status, BMI and WC. Exclusion criteria were the presence of associated disease and secondary obesity, that is, obesity due to endocrine or genetic factors. A total of 497 subjects aged 5–18 years were collected from seven different investigators.[13,15–18,29,30] After exclusion of: (1) categories of age with a small number of subjects (<10 per year or <5 per gender per year), (2) subjects lacking at least one of the required variables and, (3) ethnic groups with a low number of subjects (28 African Americans and 21 from other ethnicity), we obtained a final study group of 407 patients Caucasians and Hispanics (aged 7.0–15.9 years) (Figure 1).

Anthropometric variables (height, weight, WC) were measured according to the Anthropometric Standardization Reference Manual.[31] Body mass index (BMI) was calculated as weight (kg)/height (m^2). Sexual maturation was defined by a physician according to Tanner[32] and the subjects were classified as prepubertal (stage 1), early pubertal (stages 2–3) and late pubertal (stages 4–5). Abdominal adiposity was evaluated as VAT and SAT areas (cm^2) at lumbar L4 level (single slice), as described in detail previously by each group[12,13,15–18,29] and the VAT/SAT ratio was calculated. All the pooled studies had been approved by local Ethical Committees.

Statistical analysis
Comparisons of continuous variables between the two ethnic groups (Hispanics and Caucasians) were performed

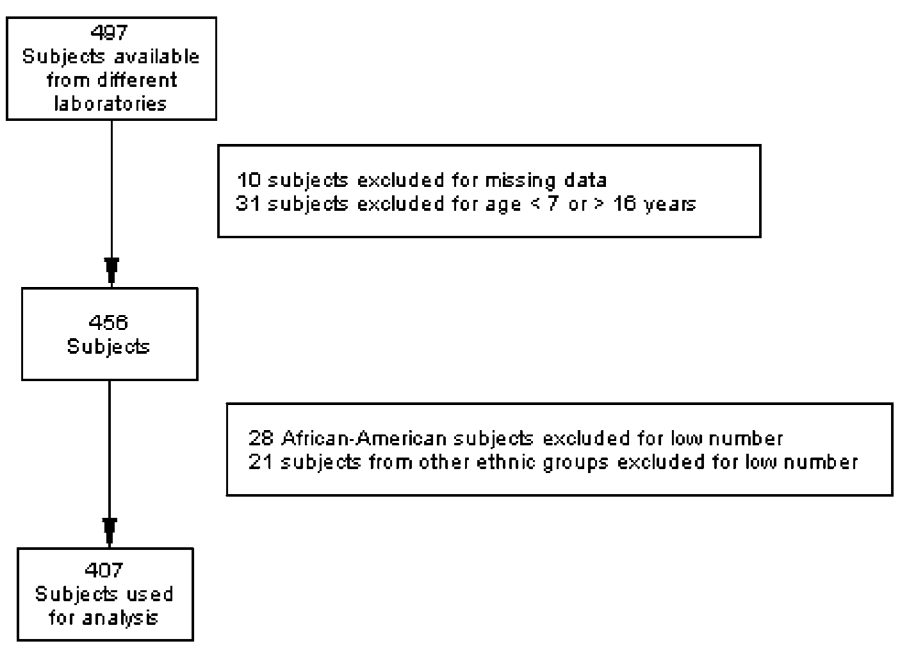

Figure 1 Flow chart of the studied subjects, from 497 collected to 407 analyzed.

by unpaired Student's t-test and those of nominal variables using the Fisher's Exact test. ANCOVA was used to test the effect of sex and race on the relationships between VAT, SAT and the predictors of interest. The contribution of the variables of interest to VAT and SAT was evaluated using the determination coefficient (R^2_{adj}) for continuous predictors and eta squared (η^2) for nominal predictors. To develop predictive equations of VAT and SAT, the sample of Hispanics and Caucasians was randomly split in two halves. The first half was used to develop a predictive equation that was then crosstested on the remaining half. R^2_{adj}, the root mean square error (RMSE) and the percent root mean square error (RMSE%) obtained from linear regression of VAT or SAT vs the variables of interest were used to determine the accuracy of the estimate. In the crossvalidation sample, the pure error (PE) of the estimate was also calculated.[33] Measured and predicted values of VAT and SAT were compared using paired t-tests. Bland–Altman plots of differences vs means coupled with analysis of the slope of the regression lines were used to ascertain the presence of bias. Statistical analysis was performed using SPSS 11.0 (SPSS, Chicago, IL, USA) and significance was set to a value of $P<0.05$ for all tests.

Results

The characteristics of the 407 subjects (178 Caucasians and 229 Hispanics) available for analysis are given in Table 1. According to Cole BMI cutoffs,[34] 65 subjects had normal weight (16%), 45 were overweight (11%) and 297 were obese (73%). There were significant between-group differences in gender (58% of Hispanics were males as compared to 47% of Caucasians) and age (Hispanics were younger) as well as in BMI and WC (Hispanics were heavier). Hispanics showed significantly higher VAT and SAT values than Caucasians ($P<0.005$). However, the VAT/SAT relationship did not differ between male and female subjects in both prepubertal ($P=0.30$) and pubertal ($P=0.75$) children (ANCOVA). Moreover, as determined by ANCOVA, VAT was similar in Caucasians and Hispanics after correction for SAT ($P=0.54$) and for BMI ($P=0.27$).

Univariate regression analysis was performed to quantify the contribution of the single variables of interest to VAT and SAT. The variance of VAT and SAT explained by anthropometry, laboratory, pubertal status, age, ethnicity and gender is given in Table 2. WC was the best single predictor of VAT, explaining 64.8% of its variance (VAT (cm^2) $= 1.1 \times$ WC (cm)-52.9) while BMI explained 56.3%. BMI was the best single predictor of SAT, explaining 88.9% of its variance (SAT (cm^2) $= 23.2 \times$ BMI (kg/m^2)-329) while WC explained 80.4%. Importantly, BMI explained a higher percentage of VAT and SAT than weight alone. The measurement of fat at different laboratories explained 16.5% of VAT and 21.4% of SAT variance ($P<0.0001$). This was partly influenced by the fact that different laboratories furnished samples of children differing for age, gender and pubertal status. Pubertal status explained 12.4 and 18.6% of VAT and SAT variance, respectively, while the contribution of age, ethnicity and gender was lower.

The contribution of ethnicity, gender, age, laboratory, pubertal status and anthropometry to the unexplained variance of the VAT–WC and SAT–BMI relationships is given in Table 3. Age, pubertal status, BMI and weight did not explain any portion of the residual VAT–WC variance and the contribution of ethnicity and gender was low ($\leqslant 3.0\%$). Likewise, ethnicity, gender, age, weight and pubertal status did not explain any portion of the residual SAT–BMI variance and the contribution of WC was trivial (1%). The addition of ethnicity and gender to the predictors did not increase the accuracy of the estimate of VAT from WC ($+1.8\%$ of the explained variance). Likewise, the addition of WC to the predictors did not increase the accuracy of the estimate of SAT from BMI. The measurement of adipose tissue at different laboratories explained 4.7 and 4.8% of the VAT–WC and SAT–BMI variance.

In order to develop predictive equations of VAT from WC and SAT from BMI, the study sample was randomly split in two halves. The first half ($n=204$) was used to develop a

Table 1 Measurements of the studied population according to ethnicity

	Hispanics	*Caucasians*	P[a]
N	229	178	
Gender (M/F)	132/97	83/95	0.028
Age (years)	11.3 ± 1.8	12.2 ± 1.8	<0.0001
Puberty (pre/early/late)	83/81/65	75/43/60	0.051
Weight (kg)	62.9 ± 19.8	56.6 ± 20.6	0.0019
Height (cm)	150 ± 12	150 ± 10	0.67
BMI (kg/m^2)	27.5 ± 5.7	24.6 ± 6.8	0.01
WC (cm)	86 ± 15	76 ± 15	<0.0001
VAT (cm^2)	44 ± 22	38 ± 22	0.0031
SAT (cm^2)	313 ± 147	235 ± 162	<0.0001

[a]Fisher's Exact test for nominal variables and Student's t-test for continous variables. VAT = visceral adipose tissue; WC = waist circumference; SAT = subcutaneous adipose tissue; BMI = body mass index.

Table 2 Variance of VAT and SAT explained by anthropometry and other variables

	VAT		*SAT*	
	Variance (%)[a]	P	*Variance (%)*[a]	P
WC	64.8	<0.0001	80.4	<0.0001
BMI	56.3	<0.0001	88.9	<0.0001
Weight	47.4	<0.0001	78.3	<0.0001
Laboratory	16.5	<0.0001	21.4	<0.0001
Pubertal status	12.4	<0.0001	18.6	<0.0001
Age	7.3	<0.0001	11.0	<0.0001
Ethnicity	2.1	0.003	5.9	<0.0001
Gender	1.8	0.006	1.2	0.026

Univariate analysis, VAT = visceral adipose tissue; WC = waist circumference; SAT = subcutaneous adipose tissue; BMI = body mass index. [a]Determination coefficient $\times$ 100 for continuous variables and $\eta^2 \times 100$ for ordinal variables.

Table 3 Variance of VAT–WC and SAT–BMI residuals explained by anthropometry and other variables

	$VAT–WC_{RES}$		$SAT–BMI_{RES}$	
	Variance (%)[a]	P	*Variance (%)*[a]	P
WC	—	—	1.0	0.042
BMI	—	0.652	—	—
Weight	—	0.369	—	0.282
Laboratory	4.7	<0.0001	4.8	<0.0001
Pubertal status	—	0.473	—	0.525
Age	—	0.249	—	0.497
Ethnicity	2.3	0.002	—	0.053
Gender	3.0	<0.0001	—	0.782

Univariate analysis, VAT = visceral adipose tissue; WC = waist circumference; SAT = subcutaneous adipose tissue; BMI = body mass index. [a]Determination coefficient × 100 for continuous variables and partial $\eta^2 \times 100$ for ordinal variables.

predictive equation that was then crossvalidated in the remaining half ($n = 203$). The VAT–WC and BMI–SAT relationships in the two samples are depicted in Figure 2. WC explained 64% of VAT variance ($P < 0.0001$) with a RMSE% of 33% (Figure 2, panel a1). The mean ± s.d. bias was $0 \pm 14\,cm^2$, corresponding to a measured value of VAT of $41 \pm 23\,cm^2$ vs an estimated one of $41 \pm 18\,cm^2$ ($P > 0.999$). The crossvalidation of the VAT equation yielded a RMSE% of 31% and a PE of $13\,cm^2$ (Figure 2, panel a2). The mean ± s.d. bias associated with the crossvalidation was $-2 \pm 13\,cm^2$, corresponding to a measured value of VAT of $42 \pm 23\,cm^2$ vs an estimated one of $40 \pm 18\,cm^2$ ($P = 0.104$). BMI explained 90% of SAT variance ($P < 0.0001$) with a RMSE% of 18% (Figure 2, panel b1). The mean ± s.d. bias was $0 \pm 49\,cm^2$, corresponding to a measured value of SAT of $280 \pm 157\,cm^2$ vs an estimated one of $280 \pm 149\,cm^2$ ($P > 0.999$). The crossvalidation of the SAT equation yielded a RMSE% of 21% and

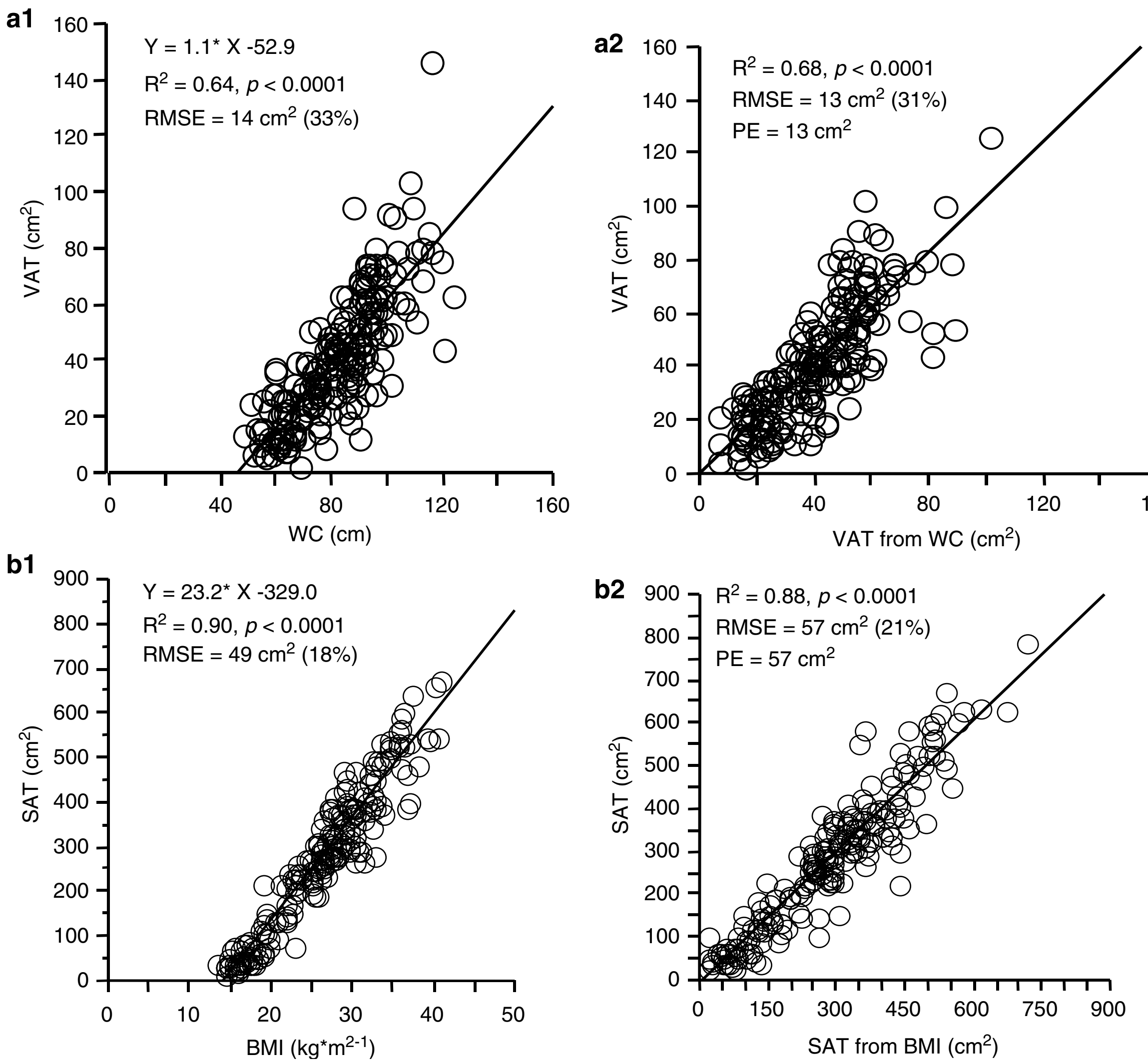

Figure 2 Generation (**a1** and **b1**, $n = 204$) and crossvalidation (**a2** and **b2**, $n = 203$) of predictive equations for VAT and SAT from WC and BMI in two random subsamples of children.

a PE of 57 cm^2 (Figure 2, panel b2). The mean ± s.d. bias associated with the crossvalidation was $1 \pm 57\,cm^2$, corresponding to a measured value of SAT of $277 \pm 161\,cm^2$ vs an estimated one of $278 \pm 146\,cm^2$ ($P = 0.853$). Figure 3 gives Bland–Altman plots of differences (anthropometry – MRI) vs means in the samples used to generate and crossvalidate the predictive equations. The slope of the fitted regression line is significantly different from 0 in all cases ($P \leqslant 0.028$), showing the existence of proportional bias. In particular, there is a tendency for anthropometry to underestimate VAT and, to a lesser degree, SAT at the highest levels of adipose tissue.

Discussion

An ideal measure of abdominal adiposity should fit the criteria of (a) being accurate in assessing the measurement, (b) being precise with small error measurement, (c) predicting risk of health consequences, (d) providing cutoffs and (e) being accessible and acceptable.[35] Actually, MRI could be considered the best measure to fit the first three criteria, while WC could be considered suitable for the last two items. In order to find the measure that could be considered as close as possible to the ideal one, we assessed the relationship between anthropometry and MRI-derived abdominal adiposity measurements in the largest pediatric sample to date. Subsequently, we investigated the effect of age, gender, puberty and ethnicity on abdominal adiposity measurement.

Adult studies have shown a higher risk of metabolic syndrome and type 2 diabetes in African American and Hispanic subjects due to difference in abdominal adiposity.[36,37] An influence of ethnicity on abdominal adiposity was also found in children.[38–40] This relationship needs to be further confirmed, as ethnic differences in clinical risk seem to be established.[41]

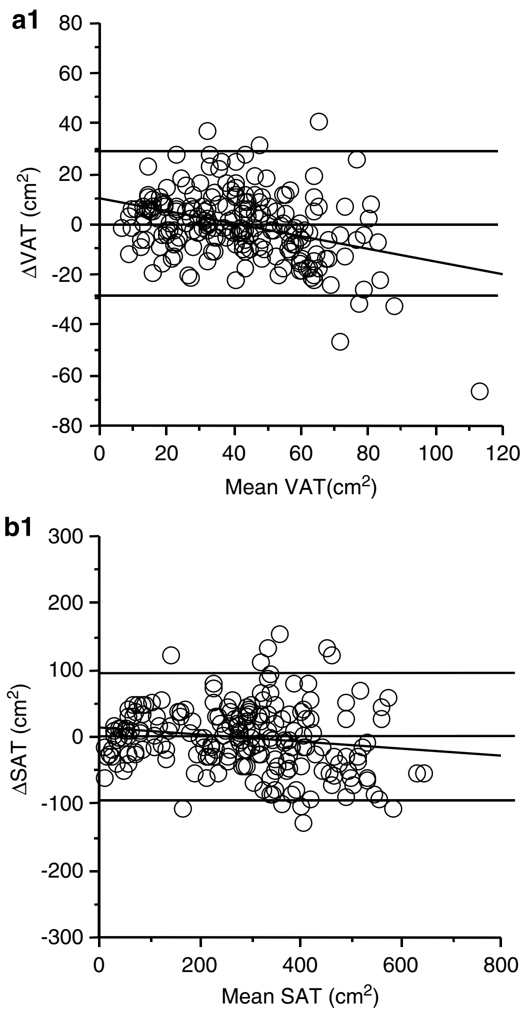

Figure 3 Bland–Altman plots of differences vs means in the samples used to generate (**a1**, **b1**) and crossvalidate (**a2**, **b2**) the predictive equations. Lines correspond to the mean ± 2 s.d. Differences are predicted values minus measured values. The slope of the fitted regression line is significantly different from 0 in all cases ($P \leqslant 0.028$), showing the existence of proportional bias.

Another important factor that influences abdominal adiposity in adults is gender. Previous studies showed that VAT/SAT is lower in females in premenopausal age while thereafter differences are less evident.[42,43] In children, gender differences in abdominal adiposity are closely linked to age- and puberty-related changes in fat distribution.[19,44–46] In our study, we found significant differences in BMI between genders and ethnic groups, underlying important differences in total adiposity. As abdominal adiposity is highly influenced by total adiposity also in children,[45] we corrected VAT for SAT and BMI in order to minimize this effect. With this approach, the influence of gender and puberty on visceral adiposity was low and the sexual dimorphism described in adults (i.e., increased VAT/SAT in males)[42,43] was not seen in subjects less than 16 years old in our analysis. This could imply that a longer observation time after completion of puberty is needed to observe this gender-related difference. Moreover, longitudinal studies of abdominal adiposity starting before puberty and conducted throughout pubertal development would be needed to confirm our cross-sectional data. Until this concept will be completely clarified, we propose that the evaluation of abdominal adiposity should not be performed without taking gender and pubertal status into consideration.

Regarding ethnicity, our analysis showed marked differences in terms of age, anthropometry and abdominal adiposity. Although ethnic differences in main outcomes were found, the impact of ethnicity on the relationship between anthropometric measures and VAT or SAT was negligible.

Anthropometry seems to be a good predictor of abdominal adiposity: WC can predict VAT, explaining about 64% of its variance and BMI can predict SAT, explaining about 90% of its variance. Janssen *et al.*[22] found similar values of variance for VAT but lower values for SAT in adults. Albeit significant ($P<0.0001$), the influence of the different laboratories on the VAT–WC and SAT–BMI relationships was low ($<5\%$), suggesting a negligible laboratory effect on the relationship between anthropometry and MRI. However, the present study was not designed to test inter laboratory CV% but to evaluate the laboratory effect on the VAT and SAT predictions by anthropometry. The heterogeneity of the samples studied at each laboratory (i.e., ethnicity, age, gender, pubertal status) could itself explain this effect, which therefore cannot be completely ascribed to measurement techniques and standardization. In fact, the similar effect for VAT and SAT is at odds with the known greater influence of the operator on the estimation of VAT than for SAT.[22]

Factors influencing the relationship between anthropometry and abdominal adiposity in our subjects can be ranked as puberty, age, ethnicity and gender (Table 2). When we analyzed the VAT–WC residuals, ethnicity and gender maintained their effect (2.3 and 3.0%, respectively) while puberty and age did not explain any variance of the residuals (Table 3). Therefore, an independent role of ethnicity on the VAT–WC relationship has to be considered, supporting the testing of ethnicity-related predictive equations in future studies.

The effect of puberty on the WC–VAT and BMI–SAT relationships could be explained by the marked physiological changes that occur during this period. During puberty there is a dramatic change in fat distribution and body proportions that BMI alone cannot describe.[46] Additionally, sex hormones differently influence SAT and VAT distribution. For example, if VAT increases and SAT decreases at the same time in a subject, the unchanged WC is ineffective in describing these modifications. The effects of puberty probably are related to gender influences, such as different levels of sex hormones between the genders. This may be true also for ethnicity, because there are differences among ethnic groups in timing, velocity and degree of pubertal development, especially in girls.[47–49]

Even if we developed equations for predicting VAT and SAT at the lumbar L4 level, a MRI single slice estimate cannot be considered a reference standard for measuring abdominal adiposity and other studies are needed employing multiple slices. The equations proposed here should nonetheless be crossvalidated in external groups to determine their accuracy. The fact that our subjects had a wide range of adiposity (27% were not obese) is a theoretical point of strength for the generalizability of these equations. However, it must be kept in mind that our equations tend to underestimate adipose tissue as VAT and SAT increase. The internal crossvalidation of the SAT algorithm was good, as an RMSE of 18% may be accepted at the population level. However, at the individual level, the use of BMI to estimate SAT should be used with caution. The crossvalidation of the VAT algorithm was acceptable, but an RMSE of 33% for the estimate of VAT from WC is relatively high both at population and individual levels. The clinical significance of this error is unclear at the moment because clinically significant cutoffs of VAT are still lacking in children. The higher RMSE for VAT from WC than for SAT from BMI may be partly due to the fact that VAT is more difficult to quantify than SAT and that WC in obese subjects is less reproducible than BMI.

In conclusion, our results elucidate the influence of ethnicity, gender, pubertal status on total and regional adiposity. WC can be considered a good predictor of abdominal adiposity according to its relationship with VAT measured by MRI, the state of the art measurement of visceral adiposity. It is important to note that the growth differences within the two races that we have studied may have had an influence on our results. Further studies with a larger number of subjects will be needed to explore the close relationship between adiposity and growth.

Acknowledgements

We especially thank Gianluca Iacobellis and other colleagues, interested in the project and ready to share their patients' data, not used in this paper due to their age.

References

1 James PT, Rigby N, Leach R. International Obesity Task Force. The obesity epidemic, metabolic syndrome and future prevention strategies. *Eur J Cardiovasc Prev Rehabil* 2004; **11**: 3–8.

2 Lobstein T, Frelut ML. Prevalence of overweight among children in Europe. *Obes Rev* 2003; **4**: 195–200.

3 Yoshinaga M, Shimago A, Koriyama C, Nomura Y, Miyata K, Hashiguchi J *et al*. Rapid increase in the prevalence of obesity in elementary school children. *Int J Obes Relat Metab Disord* 2004; **28**: 494–499.

4 Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. *JAMA* 2002; **288**: 1728–1732.

5 Ebbeling CB, Pawlak DB, Ludwig DS. Childhood obesity: public-health crisis, common sense cure. *Lancet* 2002; **360**: 473–482.

6 Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity and risk for cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *BMJ* 1984; **288**: 1401–1404.

7 Caprio S, Hyman LD, McCarthy S, Lange R, Bronson M, Tamborlane WV. Fat distribution and cardiovascular risk factors in obese adolescent girls: importance of the intraabdominal fat depot. *Am J Clin Nutr* 1996; **64**: 12–17.

8 Zhu SK, Wang Z, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. *Am J Clin Nutr* 2002; **76**: 743–749.

9 Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. *Pediatrics* 2004; **114**: 198–204.

10 Ardern CI, Janssen I, Ross R, Katzmarzyk PT. Development of health-related waist circumference thresholds within BMI categories. *Obes Res* 2004; **12**: 1094–1103.

11 de Ridder CM, de Boer RW, Seidell JC, Nieuwenhoff CM, Janeson JAL, Bakker CJG *et al*. Body fat distribution in pubertal girls quantified by magnetic resonance imaging. *Int J Obes* 1992; **16**: 443–449.

12 Fox KR, Peters DM, Armstrong N, Sharpe P, Bell M. Abdominal fat deposition in 11-year-old children. *Int J Obes* 1993; **17**: 11–16.

13 Brambilla P, Manzoni P, Sironi S, Simone P, Del Maschio A, di Natale B *et al*. Peripheral and abdominal adiposity in childhood obesity. *Int J Obes* 1994; **18**: 795–800.

14 Caprio S, Hyman LD, Limb C, McCarthy S, Lange R, Sherwin RS *et al*. Central adiposity and its metabolic correlates in obese adolescent girls. *Am J Physiol* 1995; **269**: E118–E126.

15 Brambilla P, Manzoni P, Agostini G, Beccaria L, Ruotolo G, Sironi S *et al*. Persisting obesity starting before puberty is associated with stable intraabdominal fat during adolescence. *Int J Obes Relat Metab Disord* 1999; **23**: 299–303.

16 Gower BA, Nagy TR, Goran MI. Visceral fat, insulin sensitivity and lipids in prepubertal children. *Diabetes* 1999; **48**: 1515–1521.

17 Owens S, Gutin B, Barbeau P, Litaker M, Allison J, Humphries M *et al*. Visceral adiposity tissue and markers of the insulin resistance syndrome in obese black and white teenagers. *Obes Res* 2000; **8**: 287–293.

18 Fox KR, Peters DM, Sharpe P, Bell M. Assessment of abdominal fat development in young adolescents using magnetic resonance imaging. *Int J Obes Relat Metab Disord* 2000; **24**: 1653–1659.

19 He Q, Horlick M, Fedun B, Wang J, Pierson RN, Heshka S *et al*. Trunk fat and blood pressure in children through puberty. *Circulation* 2002; **105**: 1093–1098.

20 Tershakovec AM, Kuppler KM, Zemel BS, Kats L, Weinzimer S, Harty MP *et al*. Body composition and metabolic factors in obese children and adolescents. *Int J Obes Relat Metab Disord* 2003; **27**: 19–24.

21 van der Kooy K, Seidell JC. Techniques for the measurement of visceral fat: a practical guide. *Int J Obes* 1993; **17**: 187–196.

22 Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous and visceral fat. *Am J Clin Nutr* 2002; **75**: 683–688.

23 Goran MI. Visceral fat in prepubertal children: influence of obesity, anthropometry, ethnicity, gender, diet and growth. *Am J Hum Biol* 1999; **11**: 201–207.

24 Lazarus R, Baur L, Webb K, Blyth F. Body mass index in screening for adiposity in children and adolescents: systematic evaluation using receiver operating characteristic curves. *Am J Clin Nutr* 1996; **63**: 500–506.

25 Freedman DS, Serdula MK, Srinivasan SR, Berenson GS. Relation of circumferences and skinfold thicknesses to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. *Am J Clin Nutr* 1999; **69**: 308–317.

26 Maffeis C, Pietrobelli A, Grezzani A, Provera S, Tato L. Waist circumference and cardiovascular risk factors in prepubertal children. *Obes Res* 2001; **9**: 179–187.

27 Moreno LA, Pineda I, Rodriguez G, Fleta J, Sarria A, Bueno M. Waist circumference for the screening of the metabolic syndrome in children. *Acta Pediatr* 2002; **91**: 1307–1312.

28 Bedogni G, Iughetti L, Ferrari M, Malavolti M, Poli M, Bernasconi S *et al*. Sensitivity and specificity of body mass index and skinfold thicknesses in detecting excess adiposity in children aged 8–12 years. *Ann Hum Biol* 2003; **30**: 132–139.

29 De Simone M, Verrotti A, Iughetti L, Palumbo M, Farello G, Di Cesare E *et al*. Increased visceral adipose tissue is associated with increased circulating insulin and decreased sex hormone binding globulin levels in massively obese adolescent girls. *J Endocrinol Invest* 2001; **24**: 438–444.

30 Iacobellis G, Ribaudo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A *et al*. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. *J Clin Endocrinol Metab* 2003; **88**: 5163–5168.

31 Lohman TG, Roche F, Martorell R (eds). *Anthropometric Standardization Reference Manual*. Human Kinetics: Champaign, IL, USA, 1988.

32 Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity and stages of puberty. *Arch Dis Child* 1976; **51**: 170–179.

33 Guo SS, Chumlea WC. Statistical methods for the development and testing of predictive equations. In: Roche AF, Heymsfield SB, Lohman TG (eds). *Human Body Composition*. Human Kinetics: Champaign, IL, USA, 1996, pp 191–202.

34 Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; **320**: 1240–1243.

35 Sopher A, Shen W, Pietrobelli A. Pediatric body composition. In: Heymsfield SB, Lohman TG, Wang ZM, Going S (eds). *Human Body Composition*. Human Kinetics: Champaign, IL, USA, 2005; 129–140.

36 Conway JM, Yanovski SZ, Avila NA, Hubbard VS. Visceral adipose tissue differences in black and white women. *Am J Clin Nutr* 1995; **61**: 765–771.

37 Okosun IS, Liao Y, Rotimi CN, Prewitt TE, Cooper RS. Abdominal adiposity and clustering of multiple metabolic syndrome in White, Black and Hispanic Americans. *Ann Epidemiol* 2000; **10**: 263–270.

38 Goran MI, Gower BA. Relation between visceral fat and disease risk in children and adolescents. *Am J Clin Nutr* 1999; **70**: 149S–156S.

39 Yanovski JA, Yanovski SZ, Filmer KM, Hubbard VS, Avila N, Lewis B, *et al*. Differences in body composition of black and white girls. *Am J Clin Nutr* 1996; **64**: 833–839.

40 Gutin B, Islam S, Manos T, Cucuzzo N, Smith C, Stachura ME. Relation of percentage of body fat and maximal aerobic capacity to risk factors for atherosclerosis and diabetes in black and white seven-to-eleven-year-old children. *J Pediatr* 1994; **125**: 847–852.
41 Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW *et al*. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; **350**: 2362–2374.
42 Enzi G, Gasparo M, Biondetti PR, Fiore D, Semisa M, Zurlo F. Subcutaneous and visceral fat distribution according to sex, age and overweight, evaluated by computed tomography. *Am J Clin Nutr* 1986; **44**: 739–746.
43 Seidell JC, Oosterlee A, Deurenberg P, Hautvast JGAJ, Ruijs JHJ. Abdominal fat depots measured with computed tomography: effects of degree of obesity, sex and age. *Eur J Clin Nutr* 1988; **42**: 805–815.
44 Rolland-Cachera MF. Body composition during adolescence: methods, limitations and determinants. *Horm Res* 1993; **39** (Suppl 3): 25–40.
45 Huang TT, Johnson MS, Figueroa-Colon R, Dwyer JH, Goran MI. Growth of visceral fat, subcutaneous abdominal fat and total body fat in children. *Obes Res* 2001; **9**: 283–289.
46 He Q, Horlick M, Thornton J, Wang J, Pierson Jr RN, Heshka S *et al*. Sex-specific fat distribution is not linear across pubertal groups in a multiethnic study. *Obes Res* 2004; **12**: 725–733.
47 Kaplowitz PB, Oberfield SE, the Drug and Therapeutics Executive Committees of the Lawson Wilkins Pediatric Endocrine Society. Reexamination of the age limit for the defining when puberty is precocious in girls in the United States: implication for evaluation and treatment. *Pediatrics* 1999; **104**: 936–941.
48 Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. Relation of age at menarche to race, time period and anthropometric dimensions: the Bogalusa Heart Study. *Pediatrics* 2002; **110**: e43.
49 Sus SS, Schubert CM, Chumlea WC, Roche AF, Kulin HE, Lee PA *et al*. National estimates of the timing of sexual maturation and racial differencies among US children. *Pediatrics* 2002; **110**: 911–919.