Diab. Nutr. Metab. *15:* 160-164, 2002

Association of waist circumference and body mass index with fasting blood insulin in severely obese children: A cross-sectional study

G. Bedogni*, L. Iughetti**, M. Ferrari**, M. Malavolti*, M. De Simone***, G. Fiori*, N. Battistini*, and S. Bernasconi**

ABSTRACT. **We tested whether body mass index (BMI) and waist circumference (WC) are associated with fasting insulin in severely obese children. A number of 391 (204 female and 187 male) obese children were consecutively enrolled in the study at a Paediatric outpatient clinic. They were aged 10±3 yr (mean±SD; range: 3–17 yr) and had a relative weight for age of 160±27% (mean±SD). BMI and WC explained respectively 9 and 13% of the variance of log-transformed (lt) insulin ($p<0.0001$ for both). After correction for age, however, BMI lost its association with lt-insulin (p=NS) and WC explained only 3% ($p<0.001$) of lt-insulin variance. Sex and pubertal status did not influence the relationship between WC, BMI and lt-insulin (p=NS, ANCOVA). We conclude that in severely obese children: 1) WC is a marginally better predictor of fasting blood insulin than BMI, 2) age has a substantial influence on the relationship between BMI, WC and insulin and, 3) the contribution of BMI and WC to insulin is of doubtful clinical relevance because it leaves a substantial portion (≥87%) of lt-insulin variance unexplained.**

Diab. Nutr. Metab. 15: 160-164, 2002.

INTRODUCTION

Body mass index (BMI) provides a simple measure of overweight and acts as a proxy for fat mass (FM) and morbidity and mortality risk in adults (1-3). Recently, BMI has been proposed as an adiposity index in children (4). BMI explains indeed a similar percentage of FM variance in children (20-75%) and adults (36-64%) (3-5). However, BMI is employed in adults not because of its accuracy in predicting FM but for its prognostic significance. The cut-off values for BMI have in fact been chosen on the basis of the associated risk of disease and death (6). The complications of overweight are uncommon in children but there is some evidence that childhood BMI can be used to predict adult BMI, which is known to be associated with such complications (7). This fact, along with the advantage of having just one (main) index of adiposity for all ages of life, has suggested the introduction of BMI as an adiposity index in children (4, 8). However, for BMI to be considered a prognostic indicator in children such as in adults, associations of it with clinically relevant variables have to be demonstrated. Among these variables, insulin is considered to be of central importance because of its role in the pathogenesis of the metabolic syndrome (9). The results of the Bogalusa Heart Study, conducted in children with varying degrees of adiposity, suggest that BMI is associated with blood insulin at the population level (10, 11).

Waist circumference (WC) and waist hip ratio (WHR) are indexes of body fat distribution associated with morbidity and mortality in adults (6). However, their prognostic value in children is controversial and no data are available on tracking of WC from childhood to adulthood. Based on the results of the Bogalusa Heart Study, WC has been suggested,

*Human Nutrition Chair, **Paediatrics Chair, University of Modena and Reggio Emilia, and ***Paediatrics Chair, University of L'Aquila, Italy.

Key words: Children, obesity, insulin, body mass index, waist circumference.

Correspondence to: Dr. G. Bedogni, Cattedra di Nutrizione Umana, Dipartimento di Scienze Biomediche, Facoltà di Medicina e Chirurgia, Università di Modena e Reggio Emilia, Via Campi 287, 41100 Modena, Italy. E-mail: giorgiobedogni@libero.it.

Received 8 May 2001; accepted 14 September 2001.

IGR were log-transformed (lt) to attain the normal distribution. Between-sex comparisons were performed by unpaired *t*-tests. A general linear model (GLM) was used to determine the variance contributed by anthropometric parameters (Wt, Ht, BMI, WC, HC and WHR) to lt-insulin and lt-IGR. The adjusted coefficient of determination (R^2_{adj}) and the percent root mean square error (RMSE%=root mean square error/mean value of Y) were used to quantify the accuracy of the predictions. The confounding effect of age on the anthropometric covariates was controlled by regressing each covariate against age and using the residuals of the regression as the dependent variable in the GLM. Interaction factors between each covariate and sex (X*sex) or pubertal status (X*pub) were added to the GLM to control for the confounding effect of these latter. Statistical significance was set to a value of $p<0.05$ for all tests. Values are given as mean±SD unless specified otherwise.

RESULTS

The measurements of the children are given in Table 1.

The children were aged between 3 and 17 yr and this did not differ between sexes. The majority of the enrolled children were pre-pubertal (40% female *vs* 61% male), with a lower percentage of pubertal (31% female *vs* 29% male) and late-pubertal children (29% female *vs* 10% male). Wt, Ht and BMI did not differ between sexes while RWt was higher in males than females ($p<0.05$). HC was similar in both sexes but WC and WHR were significantly higher in males than females ($p<0.0005$ and $p<0.0001$, respectively). Blood glucose was similar (p=NS) and lt-insulin higher in females than males (17 *vs* 14 μU/ml, $p<0.0005$, geometric means). Accordingly, lt-IGR was higher in females than males (0.21 *vs* 0.17, $p<0.005$, geometric means).

The variance of lt-insulin and lt-IGR explained by anthropometric dimensions is given in Tables 2 and 3 respectively.

Wt was the best single predictor of lt-insulin (R^2_{adj}=0.16) and lt-IGR (R^2_{adj}=0.13), followed by Ht (R^2_{adj}=0.14 and 0.11), HC (R^2_{adj}=0.13 and 0.12), WC (R^2_{adj}=0.13 and 0.09) and BMI (R^2_{adj}=0.09 and 0.07) ($p<0.0001$ for all values). WHR was associated neither with lt-insulin nor with lt-IGR (p=NS).

Table 2 - *Variance of (log-transformed) fasting insulin explained by anthropometric dimensions.*

	R^2_{adj}	*p*
Age	0.14	<0.0001
Wt	0.16 (0.02*)	<0.0001 (<0.005*)
Ht	0.14 (-*)	<0.0001 (NS*)
BMI	0.09 (-*)	<0.0001 (NS*)
WC	0.13 (0.03*)	<0.0001 (<0.001*)
HC	0.13 (0.02*)	<0.0001 (<0.005*)
WHR	- (NS*)	- (NS*)

*Value after correction for age. BMI: body mass index; HC: hip circumference; Ht: height; WC: waist circumference; WHR: waist/hip ratio; Wt: weight; -: absence of association.

Table 3 - *Variance of (log-transformed) insulin:glucose ratio explained by anthropometric dimensions.*

	R^2_{adj}	*p*
Age	0.11	<0.0001
Wt	0.13 (0.02*)	<0.0001 (<0.01*)
Ht	0.11 (-*)	<0.0001 (NS*)
BMI	0.07 (-*)	<0.0001 (NS*)
WC	0.09 (0.01*)	<0.0001 (<0.05*)
HC	0.12 (0.03*)	<0.0001 (<0.005*)
WHR	- (NS*)	- (NS*)

*Value after correction for age. BMI: body mass index; HC: hip circumference; Ht: height; WC: waist circumference; WHR: waist/hip ratio; Wt: weight; -: absence of association.

The regressions of lt-insulin *vs* BMI and WC are given in Figures 1 and 2, respectively. The percent root mean standard error of the estimate (RMSE%) was 20% for BMI and 21% for WC.

Since age explained 14 and 11% of lt-insulin and lt-IGR variance respectively and all anthropometric dimensions were significantly associated with age (with values of r ranging from 0.82 for WC to 0.91 for Ht, $p<0.0001$ for both), covariates were corrected for age by using linear regression. After this correction, age did not explain any variance (p=NS) of the residuals of the regression of lt-insulin and lt-IGR *vs* the age-corrected covariates.

among others, to be helpful in identifying children with "adverse" concentrations of insulin (10).
At our Outpatient Paediatric Clinic, we see mainly severely obese children who are sent from general paediatricians when traditional therapies have failed or complications of overweight have ensued (12). Thus, these children are substantially different from those enrolled in epidemiological studies, who have more variable levels of adiposity and less frequent complications. These children seemed to us to be the ideal subjects in whom to investigate the clinical relevance of the relationship between BMI, WC and insulin.

SUBJECTS AND METHODS

Subjects

A number of 391 children were consecutively enrolled in the study on their first visit at our Outpatient paediatric clinic on the basis of a relative weight for age (RWt) >120% according to the NCHS-WHO reference (13, 14). Children were classified as prepubertal (stage 1), early-pubertal (stages 2 and 3) and late-pubertal (stages 4 and 5) according to Tanner (15). The study protocol had been approved by the local Ethical Committee and the parents of the children gave their informed consent.

Anthropometry

Weight (Wt), Height (Ht), WC and hip circumference (HC) were measured following the Anthropometric Standardization Reference Manual (16). BMI was calculated as Wt (kg)/Ht (m)^2 and WHR as WC (cm)/HC (cm) (6).

Laboratory measurements

Fasting blood glucose was measured by standard methods and fasting insulin by radioimmuno-assay (Radim, Roma, Italy). The insulin:glucose ratio (IGR) was calculated as glucose (mg/dl)/insulin (μU/ml).

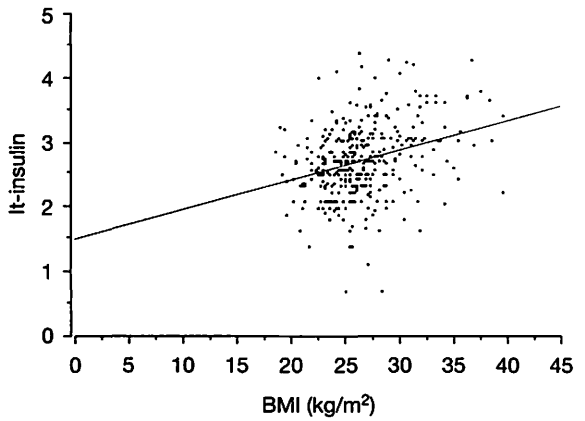
Statistical analysis

Statistical analysis was performed on a MacOS computer using the Statview 5.1 and SuperANOVA 1.1 software packages (SAS, Cary, NC, USA). All measured and calculated variables (including regression residuals) were normally distributed. Insulin and

Table 1 - *Measurements of the children.*

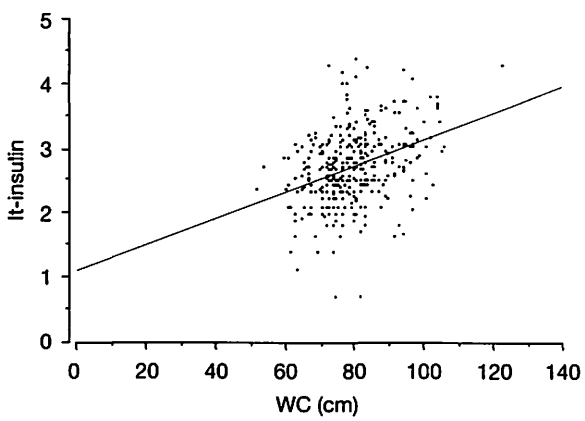
	All (no.=391)	Female (no.=204)	Male (no.=187)
Age (yr)	10±3	10±3	10±3
Pubertal status (pre-pub/early-pub/late-pub; %)	50/30/20	40/31/29	61/29/10
Wt (kg)	56±17	55±18	56±15
Ht (m)	1.43±0.15	1.42±0.16	1.43±0.14
RWt (%)	160±27	157±27*	163±26
BMI (kg/m^2)	27±4	26±4	27±4
WC (cm)	80±10	78±10°	82±10
HC (cm)	91±12	91±13	90±11
WHR	0.88±0.08	0.86±0.07°°	0.91±0.08
Glucose (mg/dl)[1]	86±12	86±12	86±12
Insulin (mU/ml)†[2]	16	17°	14
IGR†	0.19	0.21**	0.17

†Geometric mean; *p<0.05, **p<0.005, °p<0.0005, °°p<0.0001 *vs* male; [1]To convert to SI units (mmol/l), multiply by 0.05551; [2]To convert to SI units (pmol/l), multiply by 7.175. BMI: body mass index; HC: hip circumference; Ht: height; IGR: insulin/glucose ratio; RWt: relative weight;. WC: waist circumference; WHR: waist/hip ratio; Wt: weight.



Y=1.482+0.046*X; R^2_{adj}=0.09; p<0.0001; RMSE%=20%

Fig. 1 - *Relationship between log-transformed insulin and body mass index in the pooled sample of obese children (no.=391). BMI: body mass index; lt: log-transformed; RMSE%: percent root mean square error of the estimate.*



Y=1.071+0.02*X; R^2_{adj}=0.13; p<0.0001; RMSE%=21%

Fig. 2 - *Relationship between log-transformed insulin and waist circumference in the pooled sample of obese children (no.=391). lt: log-transformed; RMSE%: percent root mean square error of the estimate; WC: waist circumference.*

Correcting for age had a dramatic effect on the contribution of anthropometric variables to lt-insulin. Wt decreased its predictive power of 14% while Ht and BMI lost it completely (p=NS). Interestingly, the contribution of WC to lt-insulin resisted the correction for age but again at the expense of a substantial loss in the explained variance of this latter (-10%). The effect of sex and pubertal status, as ascertained by the X*sex and X*pub interactions, was not significant for any of the GLM.

DISCUSSION

We tested whether BMI and WC are associated with fasting insulin in a large sample of severely obese children of both sexes and different pubertal status. Our children had a mean RWt of 160%, which put them at high risk for hyperinsulinemia (6). We chose to model the relationship between anthropometric variables and insulin as continuous rather than using fixed values for hyperinsulinemia. Besides the lack of an internationally accepted definition of hyperinsulinemia in children, this was done to better appreciate the inter-individual variability of blood insulin, which is of paramount clinical importance.

In our children, WC was a marginally better predictor of lt-insulin than BMI. WC explained 4% more variance of lt-insulin than BMI but its overall contribution to lt-insulin was low (13%) and of doubtful clinical relevance. The RMSE% associated with the estimate of lt-insulin from BMI and WC was ≥20% so that this relationship cannot be safely employed for clinical purposes. The fact that the X*sex and X*pub interactions were not significant for any of the GLM suggests that the relationships between BMI, WC and insulin may be independent from sex and pubertal status in severely obese children. [This interpretation should however be made with caution because of the different number of pre-, early, and late-pubertal subjects that were (randomly) recruited in the study and because the underlying association is itself of doubtful clinical relevance].

The low accuracy of BMI and WC in predicting insulin levels in severely obese children implies that other factors should be evaluated for this role. Among these, diet and physical activity deserve a special mention because they are known determinants of insulin levels (6).

We conclude that in severely obese children: 1) WC is a marginally better predictor of fasting insulin than BMI, 2) age has a substantial influence on the relationship between BMI, WC and insulin and, 3) the contribution of BMI and WC to insulin is of doubtful clinical relevance because it leaves a substantial portion (≥87%) of lt-insulin variance unexplained.

ACKNOWLEDGEMENTS

This study was supported by a grant from Mercedes-Benz (Modena, Italy).

REFERENCES

1. Cole T.J.: Weight-stature indices to measure underweight, overweight and obesity. In: Himes J.H. (Ed), *Anthropometric assessment of nutritional status.* Wiley-Liss, New York, 1991, pp. 83-111.
2. Calle E.E., Thun M.J., Petrelli J.M., Rodriguez C., Heath C.W.: Body mass index and mortality in a prospective cohort of US adults. *N. Engl. J. Med.* 341: 1097-1105, 1999.
3. Bedogni G., Pietrobelli A., Heymsfield S.B., Borghi A., Manzieri A.M., Morini P., Battistini N., Salvioli G.: Is body mass index a measure of adiposity in elderly women? *Obes. Res.* 9: 17-20, 2001.
4. Dietz W.H., Bellizzi M.C.: Introduction: the use of body mass index to assess obesity in children. *Am. J. Clin. Nutr.* 70 (Suppl): 123S-125S, 1999.
5. Norgan N.: Anthropometric assessment of body fat and fatness. In: Himes J.H. (Ed), *Anthropometric assessment of nutritional status.* Wiley-Liss, New York, 1991, pp. 197-212.
6. World Health Organization: Obesity: preventing and managing the global epidemic. World Health Organization, Geneva, 1998.
7. Guo S.G., Chumlea W.C.: Tracking of body mass index in children in relation to overweight in adulthood. *Am. J. Clin. Nutr.* 70 (Suppl): 145S-148S, 1999.
8. Cole T., Bellizzi M.C., Flegal M., Dietz W.H.: Establishing a standard definition for child overweight and obesity worldwide: international survey. *Br. Med. J.* 320: 1-6, 2000.
9. Bellizzi M.C., Dietz W.H.: Workshop on childhood obesity: summary of the discussion. *Am. J. Clin. Nutr.* 70 (Suppl): 173S-175S, 1999.
10. Freedman D.S., Serdula M.K., Srinivasan S.R., Berenson G.S.: Relation of circumferences and skinfold thicknesses to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. *Am. J. Clin. Nutr.* 69: 308-317, 1999.
11. Srinivasan S.R., Myers L., Berenson G.S.: Temporal association between obesity and hyperinsulinemia in children, adolescents, and young adults: the Bogalusa Heart Study. *Metabolism* 48: 928-934, 1999.
12. Iughetti L., Bedogni G., Ferrari M., Pagliato E., Manzieri A., De Simone M., Battistini N., Bernasconi S.: Is fasting insulin associated with blood pressure in obese children? *Ann. Hum. Biol.* 5: 499-506; 2000.
13. Frisancho A.: *Anthropometric standards for the assessment of growth and nutritional status.* The University of Michigan Press, Ann Harbor, 1990.
14. World Health Organization: *Physical status: the use and interpretation of anthropometry.* Geneva, World Health Organization, 1995.
15. Tanner J.M.: Fetus into man. *Physical growth from conception to maturity.* Harvard University Press, Cambridge, 1978.
16. Lohman T.G., Roche A.F., Martorell R. *Anthropometric standardization reference manual.* Human Kinetics Books, Human Champaign, 1988.