

## ORIGINAL COMMUNICATION

# Waist circumference as a predictor of cardiovascular and metabolic risk factors in obese girls

C Maffei<sup>1\*</sup>, N Corciulo<sup>1</sup>, C Livieri<sup>1</sup>, I Rabbone<sup>1</sup>, G Trifirò<sup>1</sup>, A Falorni<sup>1</sup>, L Guerraggio, P Peverelli<sup>1</sup>, G Cuccarolo<sup>1</sup>, G Bergamaschi<sup>1</sup>, M Di Pietro<sup>1</sup> and A Grezzani<sup>1</sup>

<sup>1</sup>Childhood Obesity Group of the Italian Society of Pediatric Endocrinology and Diabetology, Italy

**Objectives:** (a) to explore the relationship between waist circumference and certain cardiovascular risk factors in a group of girls; and (b) to assess the clinical relevance of waist circumference in identifying girls with higher cardiovascular risk across puberty.

**Subjects and methods:** One-hundred and fifty-five overweight or obese girls aged 5–16 y were recruited. Overweight and obesity were defined on the basis of BMI, according to Cole.

**Results:** Waist circumference was significantly correlated with plasma insulin ( $r=0.43$ ;  $P<0.001$ ), systolic blood pressure ( $r=0.22$ ;  $P=0.007$ ) and  $IR_{HOMA}$  ( $r=0.40$ ;  $P<0.001$ ). A multivariate linear correlation analysis showed that, when adjusted for age and Tanner stage, waist circumference was significantly associated with plasma insulin ( $r^2=0.23$ ;  $P<0.01$ ),  $IR_{HOMA}$  ( $r^2=0.17$ ;  $P<0.02$ ), systolic and diastolic blood pressure ( $r^2=0.20$ ;  $P=0.006$  and  $r^2=0.32$ ;  $P<0.001$ , respectively). A logistic regression analysis, using  $IR_{HOMA}$  as the dependent variable, showed that waist circumference was a significant independent risk factor of insulin resistance ( $IR_{HOMA} \geq 2.6$ ) in this group of girls (OR 1.10; 95% CI 1.03–1.18;  $P=0.003$ ), independently of their age and Tanner stage.

**Conclusions:** Waist circumference of these girls was independently associated with certain cardiovascular risk factors, in particular insulin resistance and diastolic blood pressure, independently of age and Tanner stage. Thus suggesting that waist circumference may be reasonably included in clinical practice as a simple tool that may help to identify sub-groups of obese girls at higher metabolic risk across puberty.

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**Keywords:** child; obesity; cardiovascular risk factors; waist circumference

### Introduction

Obesity is a social emergency in industrialised countries (WHO, 1998). In particular, the progressive increase in the prevalence of childhood obesity is cause for concern due to the association of obesity with morbidity also in children and for the high persistency of obesity into adulthood (Must *et al*, 1992; Troiano & Flegal, 1998). Evidence that

the duration of obesity and the persistency of metabolic and cardiovascular risk factors associated with obesity increase morbidity in adulthood suggests the need for early diagnosis of obesity as well as simple and sensitive indexes of metabolic and cardiovascular risks in obese individuals early in life (Dietz & Bellizzi, 1999).

Simple anthropometric measures, such as body mass index (BMI) and waist circumference, have been used to investigate the association between adiposity and cardiovascular risk factors in adults (Lean *et al*, 1998). Recently, studies on children seem to confirm the usefulness of waist circumference as an appropriate index of metabolic and cardiovascular risk also in the pre-puberty years (Freedman *et al*, 1999; Maffei *et al*, 2001). However, few data are available for the period during puberty. Puberty affects cardiovascular and metabolic risk factors differently in males and females by the combined effects of hormones, changes of body composition and body fat distribution, and psycho-behavioural

\*Correspondence: C Maffei, Department of Pediatrics, University of Verona, Polyclinic, 37134 Verona, Italy.

E-mail: claudio.maffei@univr.it

Guarantor: Claudio Maffei, MO.

Contributors: Serone Ptlarma SpA, Via Casilina, 125 00 176, Roma, Italia.

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changes that may have relevant effects on one's lifestyle and nutritional habits.

Therefore, the purposes of the present study were: (a) to explore the relationship between anthropometric variables, lipid profile, insulin resistance index ( $IR_{HOMA}$ ) and blood pressure in a group of 154 girls aged 5–16 y; and (b) to assess the clinical relevance of waist circumference in identifying girls with higher cardiovascular risks across puberty.

## Materials and methods

### Subjects

A sample of 154 girls aged 5–16 y was recruited at Childhood Obesity Care Centres in 11 hospitals in Italy. All the girls were overweight or obese on the basis of their BMI. Each girl underwent a physical examination by a paediatric endocrinologist. None of the girls were found to have an organic cause for her obesity, and none were taking any medication that might interfere with growth and weight control. The parents of each girl gave their informed consent to participate in the study. The protocol was in accordance with the Helsinki Declaration of 1975 as revised in 1983.

### Physical characteristics

Measurements of height, weight, triceps and sub-scapular skinfolds, waist circumference and blood pressure were carried out in fasting conditions. Paediatric endocrinologists participating in the study standardized the procedure to measure anthropometric parameters. Body weight was determined to the nearest 0.5 kg on standard physician's beam scales with the girl wearing only underwear and no shoes. Height was measured to the nearest 0.5 cm on standardized, wall-mounted height boards according to the following protocol: no shoes, heels together, girl's heels, buttocks, shoulders and head touching the vertical wall surface with line of sight aligned horizontally. BMI was defined as weight/height<sup>2</sup> and was expressed in units of kg/m<sup>2</sup>. Each of the standard physician's beam scales and wall-mounted height boards used to measure the children were previously calibrated. Waist circumference was measured to the nearest cm with a flexible steel tape measure while the subjects were in the standing position at the end of gentle expiration (Lohman, 1986). The following anatomical landmarks were used: laterally, midway between the lowest portion of the rib cage and iliac crest, and anteriorly midway between the xiphoid process of the sternum and the umbilicus (Lohman, 1986). Girls were defined as obese when their BMI was higher than the BMI values for age and gender reported to pass through the adult BMI cut-off of 30, as recently suggested by Cole *et al* (2000), and overweight when their BMI was higher than the BMI values for age and gender reported to pass through the adult BMI cut-off of 25. BMI tables by Cole *et al* were used as reference. The standard deviation score of BMI was calculated for each girl. The

physician made three blood pressure measurements on the left arm over a period of 30 min with the subject supine, using a mercury sphygmomanometer. The cuffs used hand bladders long enough to circle at least half of the upper arm without overlapping, and widths that covered at least two-thirds of the upper arm. Systolic (Korotkoff phase I) and diastolic (Korotkoff phase V) blood pressure were measured three times and the average used for analysis. Puberty development was clinically assessed on the basis of Tanner stages (Tanner, 1962).

### Haemato-chemical parameters

Fasting venipuncture samples were drawn in fasting condition (12 h). The blood was immediately centrifuged and the serum obtained was frozen and stored at  $-20^{\circ}\text{C}$  for later analysis of lipid, glucose and insulin concentrations. All the samples were collected and analysed in the Laboratory of the University Hospital of Verona. Plasma glucose concentrations were measured with a glucose oxidase method. Plasma triacylglycerol and cholesterol were measured enzymatically (Abbott VP, Milan, Italy) using spectrophotometric methods (Deeg & Ziegenhorn, 1983; Nagele *et al*, 1984). Plasma high-density lipoprotein-cholesterol (HDL-ch) fraction was obtained after precipitation using phosphotungstic reagent. A 10% sample was randomly chosen each day to assess measurement error, and intra-class correlation coefficients ranged from 0.94 (HDL-ch) to 0.99 (triacylglycerol). Our core laboratory is monitored for the accuracy of total cholesterol, HDL-ch and triacylglycerol measurements. Low-density lipoprotein cholesterol (LDL-ch) was calculated using the Friedewald formula ( $\text{LDL-ch} = \text{TC} - \text{HDL-ch} - \text{triacylglycerol}/5$ ). Insulin was measured in duplicate by a specific RIA (cross reactivity with human proinsulin < 5%), using BIOSOURCE kit (Friedewald *et al*, 1972) (Fleurus, Belgium).

Insulin resistance was assessed at baseline by using the homeostasis model assessment (HOMA; Stumvoll *et al*, 2000), a method applicable to epidemiological studies. HOMA enables the examiner to estimate insulin resistance using plasma insulin and glucose. The insulin resistance index ( $IR_{HOMA}$ ) was calculated as follows:  $\text{Ins}_0$  (pmol/l)  $\times$   $\text{Gluc}_0$  (mmol/l)/135, where ' $\text{Ins}_0$ ' was the plasma insulin concentration, and ' $\text{Gluc}_0$ ' was the plasma glucose concentration, before glucose ingestion. This parameter was closely related to more accurate measurements of insulin sensitivity, such as those obtained with the glucose clamp technique, in adults with various degrees of insulin sensitivity and glucose tolerance, including type 2 diabetes (Bonora *et al*, 2000). HOMA has not been directly validated in children; however, circulating insulin levels, which are the main determinants in obtaining the HOMA score in euglycaemic subjects, are a reliable index of insulin resistance also in children, as demonstrated by the close relationship with measures obtained by using the glucose clamp (Caprio *et al*, 1996a, b).

## Statistical analysis

Data are shown as mean  $\pm$  standard deviation and range. The difference between the physical characteristics, blood pressure and biochemical parameters across the Tanner stage were analysed using the Tukey test. Zero-order correlation was performed first to assess unadjusted association between anthropometric parameters (BMI and waist circumference), blood parameters and blood pressure.

BMI and waist were correlated ( $r=0.76$ ,  $P < 0.001$ ), therefore, to avoid problems of collinearity, we ran different analyses using BMI or waist separately as independent variables. The degree of association between waist circumference, plasma lipids, insulin,  $IR_{HOMA}$  and blood pressure, adjusted for age and Tanner stage (covariates), was calculated using a multivariate linear model analysis. Several variables were not normally distributed, therefore they were expressed as their logarithm, which normalized the distributions. The same analysis was conducted using BMI as the independent variable and plasma lipids, insulin,  $IR_{HOMA}$  and blood pressure as dependent variables, adjusting for age and Tanner stage (covariates).

In order to assess the risk of insulin resistance, a multiple regression analysis using an insulin resistance index ( $\log IR_{HOMA}$ ) as the dependent variable and waist circumference, age and Tanner stage as independent variables was also run. The same analysis was conducted using BMI (logarithm), age and Tanner stage as independent variables.

To assess the effects of waist circumference on the risk of becoming insulin resistant, the children were divided into two groups based on their  $IR_{HOMA}$ : group A,  $IR_{HOMA} < 2.6$ ; group B,  $IR_{HOMA} \geq 2.6$ . We ran a multiple logistic regression analysis using  $IR_{HOMA}$  as the dependent variable and age, Tanner stage and waist circumference (quartiles) as independent variables.

In all the analyses, a probability level of  $P < 0.05$  was used to indicate statistical significance. All statistical analyses were carried out using SPSS version 9.0 software for Windows (SPSS Inc., Chicago, IL, USA) package for personal computers.

## Results

The physical characteristics of the 154 obese girls are shown in Table 1. The mean BMI was  $27.4 \pm 3.8$  (range 20.4–43.1); the mean waist circumference was  $81.9 \pm 9.2$  (range: 60–108). The haemato-chemical parameters of the total sample are shown in Table 2. The mean values of LDL-ch and  $IR_{HOMA}$  were higher than the cut-off limits conventionally used for normality. Twenty-nine percent of the girls had LDL-ch higher than 2.84 mmol/l and 75% had  $IR_{HOMA}$  higher than 2.6. The mean values of the other variables were within the normal range. However, 58% of the girls had HDL  $< 0.9$  mmol/l, 16% had total cholesterol higher than 4.65 mmol/l, 19% had diastolic blood pressure higher than the 90th centile for age and gender and 10% had systolic blood pressure higher than 90th centile. The physical char-

**Table 1** Physical characteristics and blood pressure of the 154 girls. Data are expressed as mean (s.d.) and range

	Mean (s.d.)	Range
Age (y)	11.1(1.9)	4.9–15.9
Weight (kg)	60.5 (14.1)	30.8–112
Height (cm)	147.4 (10.1)	120–171.5
BMI (kg/m <sup>2</sup> )	27.4 (3.8)	20.4–43.1
Waist (cm)	81.9 (9.2)	60–108
SBP (mmHg)	113 (12.7)	75–146
DBP (mmHg)	71 (11.5)	45–125

SBP, systolic blood pressure. DBP, diastolic blood pressure

acteristics of the girls, divided into five groups on the basis of their Tanner stage, are shown in Table 3. As expected, age, weight, height, BMI and waist circumference significantly increased across puberty ( $P < 0.01$ ). Systolic blood pressure was statistically higher ( $P < 0.05$ ) with the increase of Tanner stage, but diastolic blood pressure did not change significantly. Except for triacylglycerol ( $P < 0.03$ ), biochemical parameters were not significantly different with the increase of Tanner stage (Table 4). Interestingly, fasting insulin levels as well as  $IR_{HOMA}$  were lower in Tanner stage 5 than in the other stages, although not significantly (Table 4).

An analysis of the association between anthropometric parameters and cardiovascular risk factors showed that waist circumference was significantly correlated with BMI ( $r=0.76$ ;  $P < 0.001$ ), plasma insulin ( $r=0.43$ ;  $P < 0.001$ ), systolic blood pressure ( $r=0.22$ ;  $P=0.007$ ) and  $IR_{HOMA}$  ( $r=0.40$ ;  $P < 0.001$ ). No significant correlation was found between waist circumference and diastolic blood pressure, total cholesterol, LDL cholesterol and triacylglycerol.  $IR_{HOMA}$  also correlated with BMI ( $r=0.26$ ;  $P=0.002$ ) and triacylglycerol ( $r=0.30$ ;  $P < 0.001$ ).

A multivariate linear correlation analysis was run using waist circumference as the independent variable and total cholesterol, LDL cholesterol, triacylglycerol, insulin,  $IR_{HOMA}$ , systolic and diastolic blood pressure and HDL as dependent variables; age, and Tanner stage were used as covariates (Table 5). The analysis showed that waist circumference was significantly associated with plasma insulin ( $r^2=0.23$ ;  $P=0.002$ ),  $IR_{HOMA}$  ( $r^2=0.17$ ;  $P=0.02$ ), systolic and diastolic

**Table 2** Biochemical parameters of the 154 girls. Data are expressed as mean (s.d.) and range

	Mean (s.d.)	Range
Total cholesterol (mmol/l)	4.44 (0.74)	2.82–6.57
HDL cholesterol (mmol/l)	1.02 (0.26)	0.57–2.17
LDL cholesterol (mmol/l)	2.99 (0.68)	1.58–5.04
Triacylglycerol (mmol/l)	1.11 (0.53)	0.43–4.38
Insulin (pmol/l)	145.86 (132)	21.52–1119.3
Glucose (mmol/l)	4.49 (0.01)	2.66–6.38
$IR_{HOMA}$	4.9 (4.9)	0.57–35.1

**Table 3** Physical characteristics and blood pressure of the 154 girls divided according to their Tanner stage. Data are shown as mean (s.d.)

	Tanner 1 (n = 34)	Tanner 2 (n = 48)	Tanner 3 (n = 24)	Tanner 4 (n = 25)	Tanner 5 (n = 23)	P
Age (y)	9.1 (1.3)	10.4 (1.2)	11.5 (1.3)	12.6 (1.05)	13.7 (1.3)	< 0.001
Weight (kg)	50.8 (9.9)	55.4 (10.7)	59.5 (9.6)	71.4 (13.9)	74.4 (12.4)	< 0.001
Height (cm)	137.8 (8.6)	144.4 (7.8)	149.9 (6.2)	156.9 (6.7)	156 (7.4)	< 0.001
BMI (kg/m <sup>2</sup> )	26.5 (3)	26.6 (3.8)	26.4 (2.7)	28.8 (3.7)	30.2 (4.5)	< 0.001
Waist (cm)	80.1 (8.2)	79.9 (8.2)	81.7 (9.5)	86.7 (10.8)	84.4 (8.6)	0.02
SBP (mmHg)	107 (11)	114 (13)	114 (14)	117 (12)	117 (12)	0.01
DBP (mmHg)	67 (8)	72 (9)	70 (15)	74 (15)	74 (10)	0.1

**Table 4** Biochemical parameters of the 154 girls divided according to their Tanner stage. Data are shown as mean (s.d.)

	Tanner 1 (n = 34)	Tanner 2 (n = 48)	Tanner 3 (n = 24)	Tanner 4 (n = 25)	Tanner 5 (n = 23)	P
TC (mmol/l)	4.5 (0.9)	4.5 (0.65)	4.3 (0.5)	4.4 (0.77)	4.4 (0.85)	0.69
HDL-c (mmol/l)	1.04 (0.25)	1 (0.32)	1.03 (0.19)	0.96 (0.19)	1.08 (0.22)	0.66
LDL-c (mmol/l)	3 (0.78)	3.06 (0.66)	2.77 (0.47)	2.97 (0.69)	3.06 (0.69)	0.53
TG (mmol/l)	0.96 (0.3)	1.24 (0.56)	1.15 (0.39)	1.3 (0.82)	0.83 (0.29)	0.005
Insulin (pmol/l)	116.9 (74.8)	172.2 (192)	129.2 (67)	181.9 (145)	115.5 (48.9)	0.16
Glucose (mmol/l)	4.31 (0.5)	4.6 (0.64)	4.5 (0.63)	4.69 (0.71)	4.38 (0.62)	0.13
IR <sub>HOMA</sub>	3.68 (2.5)	5.9 (6.8)	4.1 (1.8)	6.5 (6.3)	3.7 (1.8)	0.07

blood pressure ( $r^2=0.20$ ;  $P=0.006$  and  $r^2=0.32$ ;  $P<0.001$ , respectively). The same analysis was conducted using BMI as the independent variable and plasma lipids, insulin, IR<sub>HOMA</sub> and blood pressure as dependent variables, adjusting for age and Tanner stage (covariates). BMI was associated with fasting plasma insulin ( $r^2=0.26$ ;  $P=0.03$ ) and IR<sub>HOMA</sub> ( $r^2=0.28$ ;  $P=0.02$ ) but not with the other cardiovascular risk factors.

A multiple regression analysis, using the IR<sub>HOMA</sub> (log) as the dependent variable and age, Tanner stage and waist circumference as independent variables, showed that waist circumference, adjusted for age and puberty, was able to explain inter-individual variability of the IR<sub>HOMA</sub> ( $r^2=0.16$ ;  $P<0.001$ ; Table 6). The same analysis, conducted using BMI (log) as independent variable, demonstrated that BMI,

adjusted for age and puberty, explained only 7% ( $P=0.02$ ) of the inter-individual variability of the IR<sub>HOMA</sub>.

We also ran a logistic regression analysis using IR<sub>HOMA</sub> as the dependent variable and divided the girls into two groups on the basis of their IR<sub>HOMA</sub>: group A, IR<sub>HOMA</sub> < 2.6 (non-insulin-resistant); group B, IR<sub>HOMA</sub> ≥ 2.6 (insulin resistant). Age, Tanner stage and waist circumference were the independent variables (Table 7). Waist circumference was a significant independent risk factor of insulin resistance (IR<sub>HOMA</sub> ≥ 2.6) in this group of girls (OR 1.10; 95% CI 1.03–1.18;  $P=0.003$ ). When waist circumference was included in the same analysis as categorical variable (quartiles), the group of girls with the waist in the highest quartile (> 87 cm) had more than 20 times (OR 19.14; 95% CI 2.19–166.85;  $P=0.008$ ) higher risk to have insulin resistance (IR<sub>HOMA</sub> ≥ 2.6) than the girls with the waist in the lowest quartile (< 76 cm).

**Table 5** Multivariate linear model analysis. Waist circumference was used as the independent variable and total cholesterol, LDL cholesterol, the logarithms of triacylglycerol, insulin, IR<sub>HOMA</sub>, systolic and diastolic blood pressure and HDL were used as dependent variables. Age and Tanner stage were used as covariates

Variables	F	r <sup>2</sup>	P
Total cholesterol	0.88	−0.04	0.17
LDL cholesterol	1.2	−0.02	0.6
Log HDL cholesterol	0.75	−0.08	0.85
Log triacylglycerol	1	0	0.48
Log insulin	2.06	0.23	0.002
Log IR <sub>HOMA</sub>	1.73	0.17	0.02
Log systolic blood pressure	1.86	0.20	0.006
Log diastolic blood pressure	2.62	0.32	< 0.001

**Table 6** Multiple regression analysis. Log IR<sub>HOMA</sub> was used as the dependent variable and age, Tanner stage and waist circumference were used as independent variables

	β	s.e.	P
Constant	−0.3	0.21	0.15
Waist circumference (cm)	1.25 E-02	0.003	< 0.001
Age (y)	−1.81 E-02	0.019	0.34
Tanner stage	1.99 E-02	0.03	0.44

r<sup>2</sup> of the model = 0.16;  $P<0.001$ . s.e. standard error.

**Table 7** Multiple logistic regression analysis.  $IR_{HOMA}$  was used as the dependent variable and age, Tanner stage (categorical variable) and waist circumference as independent variables

	OR	95% CI	P
Age (y)	0.73	0.49–1.10	0.13
Tanner stage (1)	1.31	0.39–4.34	0.66
Tanner stage (2)	3.46	0.63–18.95	0.15
Tanner stage (3)	5.88	0.67–51.94	0.11
Tanner stage (4)	2.04	0.22–19.122	0.53
Waist circumference (cm)	1.10	1.03–1.18	0.003

OR, odds ratio. CI, confidence interval.

## Discussion

Persistence of obesity across ages and the increasing incidence of obesity-associated morbidity also in children is a public health as well as social problem in industrialized countries (WHO, 1998). The need for early diagnosis of obesity and, possibly, of its complications has encouraged research to find simple but sensitive and accurate indexes of obesity in childhood. At the moment, BMI is the recommended index of adiposity for epidemiological studies as well as for clinical practice (Dietz & Bellizzi, 1999). The validity of BMI as an index of adiposity in children was recently demonstrated by measurements taken with dual x-ray absorptiometry (Goran *et al*, 1996; Pietrobello *et al*, 1998; Lindsay *et al*, 2001). However, BMI have some limitations. In fact, a comparison of BMI and fat mass obtained by DXA in 979 children showed that BMI, although it may describe the adiposity characteristics of a healthy paediatric population, is a poor predictor of fatness for the individual child, with a standard error for relative adiposity of 4.7–7.3% (Dietz & Bellizzi, 1999). Moreover, race can affect the level of correlation between adiposity and BMI, as demonstrated by the comparison of the BMIs of subjects from different ethnic groups having comparable body fat composition (Franklin, 1999; Daniels *et al*, 1997). Finally, the adjustment for height does not completely eliminate the stature effect so that the use of BMI in a clinical setting requires additional measures to confirm the diagnosis of obesity in children (Ellis *et al*, 1999). Moreover, studies in adults have revealed that the health risk was mainly associated with body fat distribution, more so than adiposity *per se* (Larsson *et al*, 1984). Therefore, it was suggested that anthropometric measures other than weight and height (BMI) were usable as indexes of body fat distribution and morbidity. Among these measures, waist circumference was proposed as a good index of intra-abdominal fat (Rankinen *et al*, 1999). Intra-abdominal fat is strictly associated with metabolic complications of obesity and cardiovascular risks in adults (Pi-Sunyer, 1991). In children, the relationship between intra-abdominal fat and metabolic disturbances is less evident for several reasons. First, only small amounts of intra-abdominal fat are physiologically present before adulthood (de Ridder *et al*, 1992; Goran *et al*, 1995); second, rapid changes of fat patterning are common during growth and sexual maturation with differ-

ences in the two sexes (Forbes, 1987); third, waist circumference has not yet been validated as an index of intra-abdominal fat during puberty. However, a clear relationship between intra-abdominal fat and cardiovascular risk factors has been reported in adolescents (Caprio *et al*, 1996a,b), whereas waist circumference has been shown to be a good measure for truncal fat in pre-puberty girls (de Ridder *et al*, 1992). In spite of the fact that an association between intra-abdominal fat and waist circumference has not yet been defined during puberty, the results of this study on young obese girls show that waist circumference is not just an index of obesity, but rather a better index of cardiovascular and metabolic risk factors than BMI. In fact, similarly to waist circumference, BMI is also associated with cardiovascular risk factors. However, waist and BMI have not the same predictive value. In particular, partial regression analysis revealed that  $IR_{HOMA}$  was still associated with waist ( $r=0.28$ ,  $P=0.001$ ) when the effects of BMI were removed whilst  $IR_{HOMA}$  was no longer associated with BMI ( $r=-0.02$ ,  $P=N.S.$ ) when the effects of waist were removed. Therefore, in spite of BMI being a potential predictor of cardiovascular risk factors during puberty, waist circumference seems to be a preferable parameter. Finally, to avoid problems of results interpretation due to collinearity, waist circumference and BMI were not included in the same model of multiple regression analysis.

In this study, some indexes of insulin resistance, such as  $IR_{HOMA}$  or simple plasma fasting insulin, were associated with the waist circumference of the girls. This finding is not surprising because all but five of the girls had a waist circumference above the 90th centile of the reference for age and sex. Previous studies in prepubertal children have shown that subjects with a waist circumference above the cut-off value of the 90th centile for age and sex have a high risk of obesity-related morbidity (Maffei *et al*, 2001). In addition, in our sample, more than 20% of girls had three or more metabolic or cardiovascular risk factors.

$IR_{HOMA}$  changes during puberty. Girls younger than 10y had a significantly lower  $IR_{HOMA}$  than girls older than 10y (3.58 vs 5.42;  $P=0.04$ ).  $IR_{HOMA}$  increased from Tanner 1 to Tanner 2, was pretty constant from Tanner 2 to Tanner 4 and, finally, it returned to prepubertal values at Tanner 5. This finding is in agreement with the results of the study of Moran *et al*, who performed the measure of insulin resistance by euglycemic clamp technique in a group of male and female non obese children of different ethnic origin during puberty (Moran *et al*, 1999). It is very interesting that  $IR_{HOMA}$ , which is a gross index of insulin resistance, showed the same patterns reported with the measure of glucose uptake with an accurate technique like euglycemic clamp. The variation of insulin resistance during puberty in girls may be likely explained by growth hormone/IGF-1 axis changes during puberty (Amiel *et al*, 1986; Cook *et al*, 1993).

Waist circumference was significantly associated with systolic and diastolic blood pressure, independently of age and puberty stage. This is in accordance with data reported

for obese women on whom computed tomography was used to measure intra-abdominal and subcutaneous fat to investigate the relationship between blood pressure and fat distribution (Kanai *et al*, 1990). In particular, the Authors found a correlation between the ratio of intra-abdominal visceral fat to subcutaneous fat area ratio and blood pressure, that was independent of age and BMI by multiple regression analysis.

Multiple regression analysis showed that waist circumference is a good independent predictor of insulin resistance ( $IR_{HOMA}$ ) in girls during puberty. In fact, when age and Tanner stage were used as covariates, waist circumference was able to predict 16% of inter-individual variability of  $IR_{HOMA}$ . Although the  $r^2$  value is not very high, waist was the anthropometric parameter showing the highest predictive value of  $IR_{HOMA}$ . Other factors such as fat mass, fat mass distribution, skeletal muscle and liver metabolic activity and hormones may contribute to explain part of inter-individual variability of  $IR_{HOMA}$ , which is not explained by waist. However, none of these factors may be measured during a physical examination. Moreover, logistic regression analysis showed that, adjusted for age and puberty, the increase of 1 cm of waist circumference increased the girls' risk of having an  $IR_{HOMA}$  greater than 2.6 by more than 10%, ie developing insulin resistance. Moreover, independently from age and puberty, girls with a waist circumference greater than 87 cm had more than 20 times higher probability of being insulin resistant than girls with a waist circumference smaller than 76 cm. Therefore, waist circumference in obese girls offers the opportunity to easily obtain a gross estimation of the risk of insulin resistance in these subjects. The increasing incidence of type 2 diabetes in obese adolescents and the evidence that persistency of insulin resistance is a risk factor for type 2 diabetes suggests the need for early diagnosis of insulin resistance, especially in obese children (Kanai *et al*, 1990; Lillioja *et al*, 1993; Fagot-Campagna *et al*, 2001). The measure of waist circumference may be of help in this case.

In conclusion, the waist circumference of obese girls was independently associated with certain cardiovascular risk factors, insulin resistance and diastolic blood pressure in particular, independent of age and Tanner stage. Waist circumference measurement may be a good choice in clinical practice, since it is easy to do and has a good inter-individual reproducibility; it may also help to identify sub-groups of obese girls at higher metabolic risk across puberty.

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