Can Waist Circumference Identify Children With the Metabolic Syndrome?

Valeria Hirschler, MD; Claudio Aranda, MS; Maria de Luján Calcagno, MS; Gustavo Maccalini, MS; Mauricio Jadzinsky, MD

Objective: To determine in children the association between waist circumference (WC) and insulin resistance determined by homeostasis modeling (HOMA-IR) and proinsulinemia and components of the metabolic syndrome, including lipid profile and blood pressure (BP).

Methods: Eighty-four students (40 boys) aged 6 to 13 years and matched for sex and age underwent anthropometric measurements; 40 were obese; 28, overweight; and 16, nonobese. Body mass index (BMI), WC, BP, and Tanner stage were determined. An oral glucose tolerance test, lipid profile, and insulin and proinsulin assays were performed. Children were classified as nonobese (BMI < 85th percentile), overweight (BMI, 85th-94th percentile), and obese (BMI ≥ 95th percentile).

Results: There was univariate association (P<.01) between WC and height (r=0.73), BMI (r=0.96), Tanner stage (r=0.67), age (r=0.56), systolic BP (r=0.64), diastolic BP (r=0.61), high-density lipoprotein cholesterol level (r=0.45), triglyceride level (r=0.28), proinsulin level (r=0.59), and HOMA-IR (r=0.59). Multiple linear regression analysis using HOMA-IR as the dependent variable showed that WC (β coefficient=0.050 [95% confidence interval, 0.028 to 0.073]; P=.001) and systolic BP (β coefficient=0.033 [95% confidence interval, 0.004 to 0.062]; P=.004) were significant independent predictors for insulin resistance adjusted for diastolic BP, height, BMI, acanthosis nigricans, and high-density lipoprotein cholesterol level.

Conclusion: Waist circumference is a predictor of insulin resistance syndrome in children and adolescents and could be included in clinical practice as a simple tool to help identify children at risk.

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Obese children were further classified as severely obese using the 90th percentile of BMI growth charts for US children. A BMI z score of 4 or higher was determined. Obese children were further classified as severely obese with a BMI z score of 4 or higher.

We identified 68 overweight and obese children from the population for further study using a random number table. Sixteen nonobese children were matched for sex and age with the random obese and overweight sample, and each of the 3 groups had no significant differences in BMI z score with the obese, overweight, and nonobese groups in the sample of 2202 children.

All subjects were examined by the same physician and had normal findings on physical examination except for acanthosis nigricans. They also had normal hepatic, renal, and thyroid function confirmed by measurement of aspartate aminotransferase, alanine aminotransferase, serum urea nitrogen, and thyrotropin concentrations.

The WC measurement was taken at the level of the umbilicus and recorded to 0.1 cm. A nonelastic flexible tape measure was used with the subject standing without clothing covering the waist area. The WC measures were divided into percentiles from the raw data and were entered separately for boys and girls (Table 1). Central obesity was defined as WC higher than the 90th percentile.

Arterial hypertension was defined as average systolic or diastolic BP in the 95th percentile or higher for age, sex, and height measured on at least 3 separate occasions.

Blood specimens were obtained after a 12- to 14-hour fast for determination of plasma glucose and serum lipid, insulin, and proinsulin concentrations. Plasma glucose was obtained by the glucose oxidase technique and serum lipids were measured with a Hitachi Modular P analyzer (Roche Diagnostic GmbH, Mannheim, Germany and Hitachi High-Technologies Corporation, Tokyo, Japan). Serum insulin levels were determined by radioimmunoassay (Diagnostic Products Corporation, Los Angeles, Calif) and did not cross-react with proinsulin or C-peptide (within run, 5.2%; total run, 6.8%). Proinsulin concentration was measured by a 2-site immunoluminometric assay (within run, 6%; total run, 12%).

A standard oral glucose tolerance test was administered with 1.75 g of anhydrous glucose per kilogram of body weight or a maximum of 75 g, given after the baseline blood specimens for glucose were obtained. Repeat samples for glucose were taken at 120 minutes after carbohydrate load. Impaired glucose tolerance and T2DM were defined according to the American Diabetes Association criteria.

Insulin resistance was assessed by 2 different approaches, HOMA-IR and proinsulin levels. The HOMA-IR was validated in children and adolescents and was strongly correlated with insulin resistance. The following equation for HOMA-IR index was used: (fasting insulin level \times fasting glucose level)/22.5. Proinsulin levels were measured as an index of insulin resistance. Studies of subjects without diabetes mellitus suggest that an elevated proinsulin level is more strongly associated with CVD than is hyperinsulinemia.

The study was approved by the Human Rights Committee of Durand Hospital in Buenos Aires. Each subject and parent gave written informed consent after an explanation of the study and before the initiation of the research studies.

The χ2 test was used to compare proportions. When more than 20% of the cells had expected frequencies less than 5, the Fisher exact test was used. The fit-to-normal distribution of continuous variables was assessed using the Shapiro-Wilk’s test. One-way analysis of variance (Student-Newman-Keuls post hoc test) was used when comparing more than 3 groups and with data that were normally distributed. When the homogeneity of the variances could not be proved, we used the nonparametric Kruskal-Wallis test instead of analysis of variance, with the Dunn post hoc test. To measure the strength of association between 2 variables, a Spearman rank correlation coefficient was used. Multiple linear regression analysis was performed to examine the relationship between WC and other continuous variables, such as age, BMI, BP, lipid, and/or lipoprotein levels, and HOMA-IR and proinsulin measures. P values <.05 were considered statistically significant. Data are presented as mean ± SD. Analyses were

Table 1. Clinical and Metabolic Characteristics of Study Population

<table>
<thead>
<tr>
<th></th>
<th>Nonobese (n = 16)</th>
<th>Overweight (n = 28)</th>
<th>Obese (n = 40)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>9.25 (1.48)</td>
<td>8.86 (1.99)</td>
<td>9.60 (2.63)</td>
<td>.38†‡</td>
</tr>
<tr>
<td>BMI, z score</td>
<td>−0.52 (0.93)</td>
<td>1.43 (0.22)</td>
<td>2.17 (0.27)</td>
<td>&lt;.001†§</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>15.83 (1.39)</td>
<td>21.04 (2.40)</td>
<td>27.07 (4.19)</td>
<td>&lt;.001†§</td>
</tr>
<tr>
<td>WC &gt;90th percentile, %</td>
<td>0</td>
<td>28.6</td>
<td>87.5</td>
<td>.001§</td>
</tr>
<tr>
<td>WC, cm</td>
<td>52.72 (3.67)</td>
<td>70.59 (10.30)</td>
<td>83.63 (13.09)</td>
<td>&lt;.001§</td>
</tr>
<tr>
<td>Acanthosis nigricans, No. (%)</td>
<td>4 (26.7)</td>
<td>10 (35.7)</td>
<td>23 (75.7)</td>
<td>.064‡</td>
</tr>
<tr>
<td>HDL-C level, mg/dL</td>
<td>57.81 (10.17)</td>
<td>53.66 (13.83)</td>
<td>43.78 (9.11)</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.20 (0.65)</td>
<td>1.81 (0.78)</td>
<td>2.76 (1.89)</td>
<td>&lt;.001†‡</td>
</tr>
<tr>
<td>Proinsulin level, pmol/L</td>
<td>11.68 (13.71)</td>
<td>14.59 (7.87)</td>
<td>29.35 (29.05)</td>
<td>&lt;.001§</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>97.50 (5.16)</td>
<td>102.68 (8.87)</td>
<td>109.38 (13.83)</td>
<td>&lt;.001†‡</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>61.56 (5.69)</td>
<td>64.46 (8.09)</td>
<td>71.63 (10.52)</td>
<td>&lt;.001†‡</td>
</tr>
<tr>
<td>Hypertension, No. (%)</td>
<td>0</td>
<td>0</td>
<td>10 (25)</td>
<td>.002**</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, insulin resistance by homeostasis modeling; WC, waist circumference.

SI conversion factor: To convert HDL-C to millimoles per liter, multiply by 0.0259.

*Data are expressed as mean (SD) unless otherwise indicated.
†Determined by Kruskal-Wallis test.
‡Determined by the Fisher exact test.
§No significant differences found between any of the groups.
¶Significance found between each group.
**Determined by the Fisher exact test.
Eighty-four students (44 girls) were evaluated, among whom 28 were overweight; 40, obese; and 16, nonobese. There was no difference in the mean±SD age of these 3 groups: nonobese, 9.6±2.6 years; overweight, 9.8±2.3 years; and obese, 9.6±2.6 years. Seventy-five percent of these 3 groups was nonobese, 28.6% overweight, and 16.2% obese. None had a BMI >30. Forty-four (52.4%), 20 (23.8%), 10 (11.9%), and 10 (11.9%) were Tanner stage I, II, III, and IV, respectively; mean BMI was 19.68±4.25; 20.98±4.71; 22.71±4.12; and 26.60±4.19 for nonobese, overweight, and obese groups, respectively (P<.001). Both overweight and obese groups had HOMA-IR significantly higher than the nonobese group (P<.001). The mean proinsulin levels were significantly different between groups (P<.001), with the mean proinsulin level being approximately 3-fold higher in the obese group than in the nonobese group. The systolic and diastolic BPs were higher in the obese group than in the other 2 groups (P<.001). Hypertension was present in 25% of the obese group but was present in the other 2 groups (P=.002). Mean values for clinical and laboratory findings of the different groups are shown in Table 1. Approximately 51% (n=26) of the children with WC higher than the 90th percentile vs 28% (n=12) in the group without WC higher than the 90th percentile had at least 1 additional risk factor for CVD, such as elevated BP, hyperlipidemia, or insulin resistance (HOMA-IR highest quartile; P<.01). More than 23% (n=10) in the group with central obesity had 2 or more of these risk factors and only 2.5% (n=1) in the group with WC higher than the 90th percentile.

Eighty-four students were divided into 4 groups by HOMA-IR quartiles for comparison by analysis of variance, with age and BMI z score and other variables entered as covariates. As insulin resistance increased, BMI, WC, and BP increased dramatically (P<.01). Seventeen (85%) of the 20 children in quartile 4 had WC higher than the 90th percentile vs 7 (33%) in quartile 1 (P=.003). With increasing insulin resistance, the mean proinsulin level was approximately 4 times higher in quartile 4 than in quartile 1 (Table 2).

Table 2. Clinical and Metabolic Patient Characteristics According to HOMA-IR Quartiles

<table>
<thead>
<tr>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=21)</td>
<td>(n=22)</td>
<td>(n=21)</td>
<td>(n=20)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>19.68 (4.25)</td>
<td>20.98 (4.71)</td>
<td>22.71 (4.12)</td>
</tr>
<tr>
<td>BMI z score</td>
<td>0.91 (1.39)</td>
<td>1.15 (1.25)</td>
<td>1.57 (0.73)</td>
</tr>
<tr>
<td>WC, cm</td>
<td>64.60 (9.57)</td>
<td>69.73 (12.44)</td>
<td>74.07 (10.87)</td>
</tr>
<tr>
<td>WC &gt; 90th percentile, No. (%)</td>
<td>7 (33)</td>
<td>8 (36.4)</td>
<td>11 (52.4)</td>
</tr>
<tr>
<td>Acanthosis nigricans, No. (%)</td>
<td>8 (38.1)</td>
<td>6 (28.6)</td>
<td>13 (61.9)</td>
</tr>
<tr>
<td>HDL-C level, mg/dL</td>
<td>55.40 (9.90)</td>
<td>52.45 (12.47)</td>
<td>47.60 (12.74)</td>
</tr>
<tr>
<td>Triglyceride level, mg/dL</td>
<td>72.21 (25.86)</td>
<td>62.00 (23.43)</td>
<td>95.85 (54.88)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>101.43 (9.89)</td>
<td>101.82 (7.80)</td>
<td>100.95 (6.64)</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>63.57 (8.68)</td>
<td>65.45 (8.58)</td>
<td>64.52 (6.10)</td>
</tr>
<tr>
<td>Age, y</td>
<td>8.14 (1.53)</td>
<td>8.77 (2.11)</td>
<td>9.19 (2.16)</td>
</tr>
<tr>
<td>Proinsulin level, pmol/L</td>
<td>12.13 (12.12)</td>
<td>11.23 (6.08)</td>
<td>20.48 (16.98)</td>
</tr>
</tbody>
</table>

Abbreviations: See Table 1.
SI conversion factors: To convert HDL-C to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, by 0.0113.
*Data are expressed as mean (SD) (determined by analysis of variance) unless otherwise indicated. Values for BMI, systolic BP, diastolic BP, triglyceride level, proinsulin level, and HOMA-IR increased significantly with increasing WC, whereas the HDL-C level decreased.
†Comparing quartiles 1, 2, and 3 with quartile 4.
‡Comparing quartile 1 with quartile 4.
§Comparing quartiles 1, 2, and 3 with quartile 4 and quartiles 1 and 2 with quartile 3.
\#Comparing quartile 1 with quartile 4.
\[Comparing quartiles 1 and 2 with quartile 4 and quartile 3 with quartile 2.

RESULTS

Eighty-four students (44 girls) were evaluated, among whom 28 were overweight; 40, obese; and 16, nonobese. There was no difference in the mean±SD age of these 3 groups (nonobese, 9.3±1.5 years; overweight, 8.9±2.0 years; obese, 9.6±2.6 years; P>.30). The mean±SD BMI z score of these 3 groups was nonobese, −0.52±0.9; overweight, 1.43±0.22; and obese, 2.17±0.17. None had a BMI z score of 4 or higher. Forty-four (52.4%), 20 (23.8%), 10 (11.9%), and 10 (11.9%) were Tanner stage I, II, III, and IV, respectively; mean BMI z score was not different among the 4 Tanner stage groups. Subject characteristics are depicted in Table 1. Insulin resistance increased significantly between Tanner stages I and II and remained stable through Tanner stages II, III, and IV. Two of the 84 children had impaired glucose tolerance documented by an oral glucose tolerance test; none of them were found to have T2DM.

The prevalence of WC higher than the 90th percentile was 0%, 28.6%, and 87.5% in the nonobese, overweight, and obese groups, respectively (P=.001). Both overweight and obese groups had HOMA-IR significantly higher than the nonobese group (P<.001). The mean proinsulin levels were significantly different between groups (P<.001), with the mean proinsulin level being approximately 3-fold higher in the obese group than in the nonobese group. The systolic and diastolic BPs were higher in the obese group than in the other 2 groups (P<.001). Hypertension was present in 25% of the obese group but was present in the other 2 groups (P=.002). Mean values for clinical and laboratory findings of the different groups are shown in Table 1. Approximately 51% (n=26) of the children with WC higher than the 90th percentile vs 28% (n=12) in the group without WC higher than the 90th percentile had at least 1 additional risk factor for CVD, such as elevated BP, hyperlipidemia, or insulin resistance (HOMA-IR highest quartile; P<.01). More than 23% (n=10) in the group with central obesity had 2 or more of these risk factors and only 2.5% (n=1) in the group with WC higher than the 90th percentile.

Multiple linear regression analysis using HOMA-IR as the dependent variable showed that WC and systolic BP were significant independent predictors for insulin resistance adjusted for diastolic BP, height, age, Tanner stage, acanthosis nigricans, BMI, and high-density lipoprotein cholesterol level (Table 3). Waist circumference and systolic BP explained 42.9% of the variance. To obtain an R² of 0.429 in each step, we used the stepwise method. The first step, which incorporated only WC, explained 38.9% of the total variance; the second step, which included WC and systolic BP, produced an increase of 4% of the variance, reaching 42.9%.
Acanthosis nigricans was assessed in patients, but it was not a predictive factor for insulin resistance. This suggests that WC is a predictor of insulin resistance syndrome and could be used in clinical practice as a simple tool to identify children at high risk for the later development of hypertension, dyslipidemia, and T2DM.

We have demonstrated that abdominal obesity is associated with several components of the metabolic syndrome in children. In adults, insulin resistance is associated with increased risk of both atherosclerosis and T2DM. The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) established criteria for diagnosing the metabolic syndrome in adults. Individuals with 3 or more of 5 abnormalities, including abdominal obesity (WC > 102 cm in men and > 88 cm in women), elevated BP, and elevated serum triglyceride, decreased high-density lipoprotein cholesterol, and elevated fasting glucose levels, were considered to have the syndrome. Waist circumference is a highly sensitive and specific measure of upper body fat and has been shown to correlate with insulin resistance syndrome in adults. Measurement of WC in children showed a good correlation with insulin resistance in this study and, thus, may be a valuable tool for identifying overweight and obese children who are at risk of developing metabolic and cardiovascular complications. This is further validated by studies demonstrating that children with WC higher than the 90th percentile (central obesity) are more likely to have multiple risk factors for CVD.

The dichotomous classification of WC greater than 102 cm in men and greater than 88 cm in women as a risk criterion is inconsistent with the fact that WC is a continuous variable that is positively correlated with cardiovascular risk across the entire WC range. In adults, the definition and severity of abdominal obesity is based on straightforward sex-specific threshold values related to the risk of outcomes. Children require a separate threshold of sex-specific WC norms relative to age, height, and stage of sexual maturity because of the normal increase in WC throughout childhood. Waist circumference has a low intraobserver and interobserver error, and when adjusted for clothing, accuracy remains good. Waist circumference is easy to measure and more reproducible than skinfold measurements.

The global increase in obesity in children and adolescents increases the risk for T2DM and adult CVD as components of the metabolic syndrome. The insulin resistance of obesity is considered to play a major role in the development of the metabolic syndrome. Studies in adults demonstrate that abdominal obesity and high fasting insulin levels are strong and independent predictors of later development of insulin resistance syndrome. Waist circumference is a useful measure of the abdominal obesity that is more closely related to CVD risk than is overall obesity. The present study is consistent with previous descriptions of the effects of fat distribution on risk factors for CVD in adolescents. A more central deposition of fat (android pattern) was associated with an elevation of triglyceride level, decreased high-density lipoprotein cholesterol level, increased systolic BP, and increased left ventricular mass.

The use of acanthosis nigricans as a predictive marker of hyperinsulinemia has become a common practice. Previous studies have associated the presence of acanthosis nigricans with high insulin levels, thus identifying a subgroup believed to be at greater risk for T2DM. Acanthosis nigricans was proposed by the American Diabetes Association as an insulin resistance marker and an independent risk factor for T2DM in children. On the other hand, several studies found that all of the measures of body adiposity were superior to acanthosis nigricans for the diagnosis of insulin resistance. Use of acanthosis nigricans as the sole indicator of hyperinsulinemia led physicians to miss the diagnosis in half of all children with significant hyperinsulinemia. Consistent with these results, we found that acanthosis nigricans was not a predictive factor for insulin resistance.

In our study, there was a significant correlation between WC and all the components of the metabolic syndrome. Multiple linear regression analysis using HOMA-IR as the dependent variable showed that WC and systolic BP were independent predictors for insulin resistance, when adjustment was made for other variables. Insulin resistance was predicted by WC and systolic BP, which

<table>
<thead>
<tr>
<th>Model</th>
<th>β Coefficient</th>
<th>Standard Error</th>
<th>t Test</th>
<th>P Value</th>
<th>95% Confidence Interval</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>−5.055</td>
<td>1.228</td>
<td>−4.118</td>
<td>.001</td>
<td>−7.500 to 2.609</td>
<td>0.429</td>
</tr>
<tr>
<td>WC</td>
<td>0.050</td>
<td>0.011</td>
<td>4.401</td>
<td>.001</td>
<td>0.028 to 0.073</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.033</td>
<td>0.015</td>
<td>2.289</td>
<td>.04</td>
<td>0.004 to 0.062</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BP, blood pressure; HOMA-IR, insulin resistance by homeostasis modeling; WC, waist circumference.

*Dependent variable, HOMA-IR.
explained 42.9% of the total variance. In adults, insulin resistance drives the processes underlying the metabolic syndrome.30 Visceral obesity may be an important risk factor for insulin resistance syndrome in children. Waist circumference serves as a readily available means to estimate abdominal obesity in the office setting. Normative data specific for ethnic group need to be collected. The present study showed that children with abdominal obesity, as determined by WC, have increased metabolic risk factors for CVD and T2DM. Because this study is cross-sectional, longitudinal studies will be needed to determine the significance of our observations.

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REFERENCES