Effect of Android to Gynoid Fat Ratio on Insulin Resistance in Obese Youth

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Background: Upper body fat distribution is associated with the early development of insulin resistance in obese children and adolescents.

Objective: To determine if an android to gynoid fat ratio is associated with the severity of insulin resistance in obese children and adolescents, whereas peripheral subcutaneous fat may have a protective effect against insulin resistance.

Setting: The pediatric department of University Hospital, Clermont-Ferrand, France.


Participants: Data from 66 obese children and adolescents coming to the hospital for medical consultation were used in this study.

Main Outcome Measures: Subjects were stratified into tertiles of android to gynoid fat ratio determined by dual-energy x-ray absorptiometry. Insulin resistance was assessed by the homeostasis model of insulin resistance (HOMA-IR) index.

Results: There were no differences in weight, body mass index, and body fat percentage between tertiles. Values of HOMA-IR were significantly increased in the 2 higher tertiles (mean [SD], tertile 2, 2.73 [1.41]; tertile 3, 2.89 [1.28]) compared with the lower tertile (tertile 1, 1.67 [1.24]) of android to gynoid fat ratio (P < .001). The HOMA-IR value was significantly associated with android to gynoid fat ratio (r = 0.35; P < .01).

Conclusions: Android fat distribution is associated with an increased insulin resistance in obese children and adolescents. An android to gynoid fat ratio based on dual-energy x-ray absorptiometry measurements is a useful and simple technique to assess distribution of body fat associated with an increased risk of insulin resistance.

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lescents with a high visceral to subcutaneous fat ratio exhibit an impaired glucose tolerance in comparison with those with a low ratio. Moreover, there are several reports in obese children and adolescents showing that ectopic fat storage and hypertriglyceridemic waist are associated with declined insulin sensitivity. Weiss et al. have shown that the development of severe peripheral insulin resistance in obese children and adolescents with impaired glucose tolerance was closely associated with intramyocellular and intra-abdominal lipid accumulation. A high intramyocellular lipid deposition has been shown to occur early during childhood and adolescence in association with peripheral insulin resistance. Most studies investigating metabolic alterations in relation with regional fat deposition have focused on subcutaneous abdominal, visceral, or thigh fat depots. Dual-energy x-ray absorptiometry (DXA) measurements have been used in several studies to assess regional body fat distribution in children and the association with cardiovascular risk factors. Moreover, there is a good agreement between magnetic resonance imaging measurements of abdominal adipose tissue and DXA fat measurements. Little attention has been paid to the association between gynoid fat storage and insulin resistance in obese children. In this study, we attempted to determine if the ratio between abdominal, or android fat pattern, and lower limb fat percentage, or gynoid fat pattern, determined by DXA scan was associated with the severity of insulin resistance assessed by the homeostasis model of insulin resistance (HOMA-IR) index. We hypothesized that children with a high android to gynoid fat ratio would exhibit an impaired glucose tolerance in comparison with those with a low ratio.

METHODS

Participants in this study were 66 obese children and adolescents (31 girls and 35 boys) and their parents coming to the Department of Pediatrics, University Hospital, Clermont-Ferrand, France, for medical consultation. Parents and children who agreed to take part to the study signed an informed consent. The experimental protocol of this study was approved by the local ethics committee (Comité de Protection des Personnes, Sud Est IV). Children included in this study were younger than the 95th percentile of body mass index (BMI) for age and sex defined by the International Obesity Task Force.

Medical examination and anthropometric measurements were performed for each subject by a pediatrician. Body mass was measured to the nearest 0.05 kg with a digital scale (model 873; Seca Omega, Hamburg, Germany). Height was measured with a standing stadiometer and recorded with a precision of 1 mm. Body mass index was calculated as weight in kilograms divided by height in meters squared. Body mass index and waist circumference z scores were calculated for age and sex reference values. Waist circumference was measured in a standing position with a nonelastic tape that was applied horizontally midway between the costal arch and the iliac crest. All subjects were free of medication known to affect energy metabolism and none of the subjects had evidence of significant disease, non-insulin-dependent diabetes mellitus, or other endocrine disease.

BODY COMPOSITION

Body composition was determined by DXA scan (QDR 4500 x-ray densitometer; Hologic, Waltham, Massachusetts) and version 9.10 of total body scans software (Hologic Inc, Bedford, Massachusetts). Children were asked to lie down in a supine position on the DXA table and to stay still until the end of the scanning procedure. They were also instructed to keep their arms separated from their trunk and their legs separated from one another.

Percentage of abdominal fat was determined manually by an experienced experimenter by drawing a rectangular box around the region of interest between vertebral bodies L1 and L4. The upper limit was set with the horizontal line going through the T2/L1 vertebral space and the lowest limit was set with a horizontal line going through the L4/L5 vertebral space. Data were analyzed with Hologic QDR software for Windows (version 12.6), which integrates whole-body measurement and standard body regions, such as the trunk, arms, and legs, delineated by specific anatomical landmarks. Gynoid fat deposition was assessed by lower limb fat percentage. Android to gynoid fat ratio was determined by using fat percentage in lower limbs and in the abdominal region. To test the hypothesis that an android to gynoid fat ratio is associated with an impairment of insulin sensitivity, study subjects were grouped into tertiles. We used tertiles to ensure a number of subjects in each subgroup sufficient to give meaningful results.

BLOOD SAMPLES

Blood samples were drawn between 8 AM and 10 AM in a fasted state from an antecubital vein. Samples were centrifuged (at 4000 g for 10 minutes at 4°C) and plasma was transferred into plastic tubes and kept at −80°C until analysis. The plasma glucose concentration was determined by enzymatic methods (Modular P900; Roche Diagnostics, Meylan, France). Plasma insulin concentration was assayed by a chemiluminescent enzyme immunoassay on an Immulite 2000 (Diagnostic Products Corporation, Los Angeles, California).

Two indexes of insulin resistance were calculated from glucose and insulin concentrations. The HOMA-IR index was calculated as (fasting insulin level × fasting glucose level)/22.5 and quantitative insulin-sensitivity check index, as 1/(log fasting insulin level + log fasting glucose level).

STATISTICAL ANALYSIS

Results are expressed as mean (SD). Normality of the distribution was checked with the Kolmogorov-Smirnov test for each variable. Dependent variables were compared between the 3 groups by using a 1-way analysis of variance. Android to gynoid fat ratio and abdominal fat percentage were similar between boys and girls in the 3 groups. Hence, boys and girls were grouped together in each tertile.

Spearman correlation coefficients were used to describe associations between continuous variables. We also used a multiple stepwise regression to explain the variance of HOMA-IR values. Age, waist circumference z score, BMI, body fat percentage, and the android to gynoid fat ratio were included as independent variables.

All statistical analyses were carried out with Statview software, version 5.0 (Abacus Concepts, Berkeley, California). Statistical significance was set at P < .05.
RESULTS

DESCRIPTIVE STATISTICS OF THE SAMPLE

Descriptive results of the population are presented for boys and girls in Table 1. Body mass, percentage of body fat, and lean body mass were similar in the 3 tertiles. Tertiles were also similar for the number of boys and girls. Because of the study design, the android to gynoid fat ratio was significantly different between the 3 tertiles (P<.001 for all comparisons). There were significant differences for percentage of abdominal fat between tertiles 1 and 2 (P<.001) and tertiles 1 and 3 (P<.001). There was no significant difference for percentage of fat mass in lower limbs between tertiles.

INDEXES OF INSULIN RESISTANCE: FASTING GLUCOSE AND INSULIN CONCENTRATIONS

Mean (SD) HOMA-IR values were significantly higher in tertiles 2 (2.73 [1.41]) and 3 (2.89 [1.28]) than in tertile 1 (1.67 [1.24]) (P=.009 and .003, respectively). Mean (SD) quantitative insulin-sensitivity check index values were also significantly higher in tertile 1 (0.37 [0.04]) than in tertiles 2 (0.34 [0.03]) and 3 (0.33 [0.02]) (P=.005 and P=.001, respectively). Differences were not significant between tertiles 2 and 3. Results are shown in Figure 1 and Figure 2.

Mean (SD) fasting plasma glucose level was not significantly different between tertiles (tertile 1, 85.79 [4.30] mg/dL; tertile 2, 88.79 [6.59] mg/dL; tertile 3, 89.28 [7.50] mg/dL), whereas mean (SD) insulin concentration was significantly higher in tertiles 2 (12.39 [6.12] mU/L) and

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**Table 1. Descriptive Statistics of the Population**

<table>
<thead>
<tr>
<th>Tertile</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>9</td>
<td>11</td>
<td>11</td>
<td>.07</td>
</tr>
<tr>
<td>F</td>
<td>14</td>
<td>12</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>9.61 (2.70)</td>
<td>11.21 (2.27)</td>
<td>11.11 (2.37)</td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>57.00 (29.42)</td>
<td>65.33 (24.43)</td>
<td>61.65 (19.03)</td>
<td>.31</td>
</tr>
<tr>
<td>BMI</td>
<td>24.46 (5.82)</td>
<td>27.94 (5.74)</td>
<td>27.23 (4.94)</td>
<td>.09</td>
</tr>
<tr>
<td>BMI z score</td>
<td>1.91 (0.40)</td>
<td>2.05 (0.38)</td>
<td>1.94 (0.47)</td>
<td>.51</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>36.84 (5.38)</td>
<td>38.75 (6.34)</td>
<td>38.63 (4.48)</td>
<td>.41</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>78.96 (16.50)</td>
<td>89.23 (17.15)</td>
<td>90.15 (12.73)</td>
<td>.07</td>
</tr>
<tr>
<td>Waist circumference z score</td>
<td>1.94 (0.74)</td>
<td>2.35 (0.57)</td>
<td>2.55 (0.56)</td>
<td>.05</td>
</tr>
<tr>
<td>Abdominal fat, %</td>
<td>30.36 (4.18)</td>
<td>37.24 (6.62)</td>
<td>40.43 (5.11)</td>
<td>.001</td>
</tr>
<tr>
<td>Truncal fat mass, %</td>
<td>32.38 (5.53)</td>
<td>36.22 (5.94)</td>
<td>34.81 (5.27)</td>
<td>.08</td>
</tr>
<tr>
<td>LBM, kg</td>
<td>33.37 (15.24)</td>
<td>37.86 (11.34)</td>
<td>40.81 (14.21)</td>
<td>.21</td>
</tr>
<tr>
<td>Lower limb fat, %</td>
<td>43.82 (6.28)</td>
<td>43.63 (7.79)</td>
<td>40.00 (5.01)</td>
<td>.09</td>
</tr>
<tr>
<td>Android to gynoid fat ratio</td>
<td>0.70 (0.07)</td>
<td>0.86 (0.05)</td>
<td>1.01 (0.04)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); LBM, lean body mass.

a Protected least significant difference Fisher test for comparison between groups: significant difference between tertile 1 and tertile 3, P<.05.

b Protected least significant difference Fisher test for comparison between groups: significant difference between tertile 1 and tertile 2, P<.001; tertile 1 and tertile 3, P<.001; and tertile 2 and tertile 3, P<.05.

c Protected least significant difference Fisher test for comparison between groups: significant difference between tertile 1 and tertile 2, P<.001; tertile 1 and tertile 3, P<.001; and tertile 2 and tertile 3, P<.001.

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**Figure 1.** Mean (SD) homeostasis model of insulin resistance (HOMA-IR) index values in tertiles of android to gynoid fat ratio. *P<.001.

**Figure 2.** Mean (SD) quantitative insulin-sensitivity check index (QUICKI) values in tertiles of android to gynoid fat ratio. *P<.001.
HOMA-IR value (respectively). Adjusted The multiple stepwise regression showed that age and
with fasting glucose concentration. The fat distribution variables had significant correlation
variables or glucose and insulin concentrations. None of
age were significantly correlated with insulin sensitivity
Neither body fat percentage nor lower limbs fat percent-
percentage of abdominal fat correlated positively with
Our hypothesis was that a preferential fat storage at the
3 (13.04 [5.20] mU/L) than in tertile 1 (7.91 [5.68] mU/L)
Differences were not significant between tertiles 2 and 3 (P = .70).

CORRELATION COEFFICIENT

Relationships between fat distribution variables and in-
sulin sensitivity variables are shown in Table 2. Per-
centage of abdominal fat correlated positively with
HOMA-IR value (r = 0.34; P < .01). The android to gy-
noid fat ratio was positively correlated with HOMA-IR
value (r = 0.35; P < .01). Android to gynoid fat ratio was
also significantly and positively correlated with fasting
insulin concentration (r = 0.34; P < .01). Waist circum-
ference and waist circumference z score were signifi-
cantly correlated with HOMA-IR value (r = 0.44; P < .001
and r = 0.33; P < .01). Body mass index was correlated with
HOMA-IR value (r = 0.45; P < .001) but not BMI z score.
Neither body fat percentage nor lower limbs fat percentage
were significantly correlated with insulin sensitivity
variables or glucose and insulin concentrations. None of
the fat distribution variables had significant correlation
with fasting glucose concentration.

MULTIPLE STEPWISE REGRESSION

The multiple stepwise regression showed that age and
the android to gynoid fat ratio were significant predic-
tors of HOMA-IR value (β coefficients were 0.26 and 2.28,
respectively). Adjusted R² was 0.30. Body mass index,
waist circumference z score, and body fat percentage were
not significant predictors of HOMA-IR value.

COMMENT

Our hypothesis was that a preferential fat storage at the
abdominal level rather than in the lower limbs would be
associated with increased insulin resistance. To this aim,
we calculated a simple index of android to gynoid fat dis-
tribution as a ratio between percentage of abdominal fat
and percentage of lower limbs fat based on DXA mea-
surements. Insulin resistance was estimated by using
simple indexes based on fasting plasma glucose and in-
sulin concentrations. Indexes such as HOMA-IR and the
quantitative insulin-sensitivity check index calculated
from fasting samples have been shown to be valid to as-
sess insulin resistance during puberty when compared with
direct measurement with a glucose clamp. The main finding
was that insulin resistance was increased in children with
central rather peripheral fat deposits in groups matched for
body mass and percentage of body fat. Furthermore, insulin resistance was associated with
abdominal adiposity without distinction between sub-
cutaneous and visceral fat depots. However, although
HOMA-IR values increased from the lowest tertile to
tertiles 2 and 3, whereas there was no significant differ-
cence between tertiles 2 and 3, a linear regression be-
tween the android to gynoid fat ratio and HOMA-IR value
did not provide a threshold value of android to gynoid
fat ratio above which obese children have an increased
risk of insulin resistance.

Indeed, in the present study, there was no signifi-
cant association between percentage of body fat and
insulin resistance. Previous studies have shown in
young subjects that the degree of obesity is associated
with a worsening of all the components of the meta-
abolic syndrome, including insulin resistance. Several
points can explain the lack of correlations between
percentage of body fat and indexes of insulin resis-
tance in the present study. Despite a similar degree of
obesity, a lower prevalence of impaired glucose toler-
ance and type 2 diabetes have been reported in Euro-
pean than in American children. Indeed, even
though impaired fasting glucose concentration may
not be sensitive enough to detect impaired glucose tol-
erance, only 2 children had a fasting glucose concen-
tration higher than 100 mg/dL. Hence, together with a
reduced number of subjects with severe obesity in
comparison with other studies, only mild alterations
of insulin sensitivity may explain the lack of associa-
tion between percentage of body fat and insulin resis-
tance. The development of abdominal obesity during
puberty may be favored by pubertal insulin resistance
and its consequent hyperinsulinemia. A limitation of
this study is that data analysis was based on age rang-
ing between 6 and 17 years and not on direct assess-
ment of pubertal stages. Logically, age was a signifi-
cant predictor of insulin resistance. Moreover, the

Table 2. Correlation Coefficients for Association Between Fat Distribution Variables and Markers of Insulin Resistance

<table>
<thead>
<tr>
<th>Variable</th>
<th>HOMA-IR</th>
<th>QUICKI</th>
<th>Plasma Glucose Level</th>
<th>Plasma Insulin Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal fat, %</td>
<td>0.34a</td>
<td>-0.36a</td>
<td>0.12</td>
<td>0.34a</td>
</tr>
<tr>
<td>Lower limb fat, %</td>
<td>0.04</td>
<td>0.01</td>
<td>0.08</td>
<td>0.05</td>
</tr>
<tr>
<td>Android to gynoid fat ratio</td>
<td>0.35a</td>
<td>-0.41a</td>
<td>0.20</td>
<td>0.34a</td>
</tr>
<tr>
<td>BMI z score</td>
<td>0.45b</td>
<td>0.46a</td>
<td>0.13</td>
<td>0.47a</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.22</td>
<td>0.22</td>
<td>0.24</td>
<td>0.22</td>
</tr>
<tr>
<td>Waist circumference z score</td>
<td>0.44a</td>
<td>0.52a</td>
<td>0.06</td>
<td>0.48a</td>
</tr>
<tr>
<td>Lower limb fat, %</td>
<td>0.04</td>
<td>-0.19</td>
<td>0.00</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HOMA-IR, homeostasis model of insulin resistance index; QUICKI, quantitative insulin-sensitivity check index.

a P < .01.
b P < .05.
c P < .001.
effect of puberty was partly controlled by the use of age- and sex-specific BMI and waist circumference growth charts.

Several studies have already used DXA to provide measurements of abdominal fat mass. Measurement by DXA of central adiposity from L1 to L4 has previously been shown to be associated with insulin resistance in adults and to be a valid alternative to other techniques. However, a limitation of the present study is that abdominal fat determined by DXA does not allow the distinction between visceral and subcutaneous abdominal tissues. Bacha et al observed that in 2 groups of obese adolescents with a similar percentage of body fat (42.5 and 44.2) those who had the lowest visceral fat area and the lowest subcutaneous fat area at L4-L5 exhibited only a moderate insulin resistance. On the other hand, Maffeis et al recently showed that visceral adipose tissue area was not associated with insulin sensitivity, but may rather alter insulin sensitivity through its effect on liver fat content, which explained 16% of the variation in insulin sensitivity in obese children. Hence, questions remain about the importance of visceral fat for the development of insulin resistance. Finally, significant correlations between waist circumference or waist circumference z score and HOMA-IR confirm that simple anthropometric measurements are also reliable to assess an association between upper body adiposity and insulin resistance.

We did not observe any association between lower body fat percentage and insulin resistance. This result is similar to previous findings in adults. Although subcutaneous adipose tissue stores approximately 90% of thigh fat, it is other compartments quantitatively minor for fat storage, such as intramuscular triglycerides, that are significantly associated with insulin resistance. In obese children, both intramyocellular and extramyocellular triglycerides stores are associated with central adiposity, suggesting that deposition of fat in these tissues is interdependent. Meanwhile, an important leg fat storage, almost at the subcutaneous level, reflects the ability of this depot to be a metabolic sink for excess energy intake, thereby preventing ectopic accumulation. Together, android to gynoid ratio and age explained 30% of the variance of insulin resistance. Fitness level, which was not assessed in the present study, has important effects on indexes of insulin sensitivity even in obese children and may be a factor that could also explain an important part of variability of insulin resistance in our population.

To conclude, the present study showed that an android rather than a gynoid fat distribution was associated with an increased insulin resistance in obese children and adolescents. Hence, an android to gynoid fat ratio based on DXA measurement may be a useful and simple technique to assess a pattern of body fat distribution associated with an increased insulin resistance. This study also confirmed that the severity of insulin resistance is associated with abdominal obesity, which can be assessed by waist circumference measurement, whether fat is located essentially in visceral or subcutaneous adipose tissue in children and adolescents.


Archives of Pediatrics and Adolescent Medicine will devote their May 2010 issue to papers on the effects of life experiences occurring during the critical window of birth to age 5 years on the emotional and psychological health and development—or ill health—of children both during that age and at later ages during childhood and adolescence. Papers submitted by September 30, 2009, have the best chance of acceptance.