Association of Body Fat Distribution and Cardiovascular Risk Factors in Children and Adolescents

Stephen R. Daniels, MD, PhD; John A. Morrison, PhD; Dennis L. Sprecher, MD; Philip Khoury, MS; Thomas R. Kimball, MD

Background—Obesity is associated with increased risk of cardiovascular disease in adults and less favorable cardiovascular risk factor status in children and adolescents. In adults, fat distribution has been shown to be related to lipid and lipoprotein concentrations, blood pressure levels, and left ventricular mass. These relationships have not been extensively studied in young subjects.

Methods and Results—This was a cross-sectional study of 127 children and adolescents 9 to 17 years of age. Dual-energy x-ray absorptiometry was used to measure total and regional fat mass. The dependent variables were fasting lipid and lipoprotein concentrations, systolic and diastolic blood pressures, and left ventricular mass. There were significant ($P<0.05$) univariate correlations between fat distribution and log triglycerides ($r=0.27$), log HDL cholesterol ($r=0.26$), and left ventricular mass ($r=0.37$). Multiple regression analysis showed that the significant independent correlates for triglycerides and HDL cholesterol were age and fat distribution; for systolic blood pressure, height and fat distribution; and for left ventricular mass, height, race, sex, and fat distribution.

Conclusions—These results demonstrate that fat distribution is a more important independent correlate of cardiovascular risk factors than percent body fat in children and adolescents. Greater deposition of central fat (an android fat pattern) is associated with less favorable plasma lipid and lipoprotein concentrations, blood pressure, and left ventricular mass.

Key Words: obesity ■ risk factors ■ cholesterol ■ blood pressure

Obesity is associated with increased risk of cardiovascular disease in adults and with less favorable cardiovascular risk factor status in children and adolescents.$^{1,2}$ Recently, it has also been suggested that fat distribution may be important in determining risk of cardiovascular disease. An android fat pattern with excess fat in the upper (central) body region, particularly the abdomen, has been associated with increased risk compared with the gynoid pattern, with increased fat in the lower body segment, particularly the hips and thighs.$^{3,4}$

Most previous studies of fat distribution have used indirect anthropometric methods, such as skin-fold thickness, circumferences, and waist-to-hip ratio, to estimate the pattern of fat distribution. The technique of dual-energy x-ray absorptiometry (DEXA) has been shown to provide a direct, accurate, and precise measure of lean body mass and total fat mass. This method has been validated against a range of established techniques, including underwater weighing.$^{5}$ This method also allows quantification of fat mass in anatomically defined regions of interest,$^{6}$ which allows more precise evaluation of the impact of fat distribution.

The purpose of this study was to evaluate the effect of adiposity and fat distribution on established cardiovascular risk factors in children and adolescents. The dependent variables were lipid and lipoprotein concentrations, systolic and diastolic blood pressures, and left ventricular mass.

Methods
This was a cross-sectional study of subjects 9 to 17 years of age. Study subjects included boys and girls, black and white, who were recruited from local schools. Subjects were recruited to achieve an appropriate sample size for each of the race and sex groups. Subjects were included after informed consent was obtained from the parent or legal guardian. This study was approved by the Institutional Review Board of the Children’s Hospital Medical Center, Cincinnati, Ohio.

Dual-Energy X-Ray Absorptiometry
DEXA measurements were performed with a Hologic Inc 1000/W device for quantification of bone mineral density, lean mass, and fat mass. This method uses 2 beams of low-energy x-rays that are collected by the external detector after attenuation by the body tissue through which they have passed. Soft tissue is resolved by use of mass attenuation coefficients derived from tissue equivalent standards for fat-free and fat tissue. DEXA has been shown to provide accurate and precise measurements of bone mineral content, fat-free mass, and fat mass in subjects over a wide range of ages and body size.$^{6-8}$ DEXA has been validated in adults and children against the
hydrodensitometry method, which has previously been established as the most valid measurement of lean body mass and fat mass. To evaluate the effects of total body adiposity, percent body fat was used. Percent body fat was calculated as total body fat mass divided by total body mass times 100. To evaluate the effects of fat distribution, 4 regions of interest were manually determined. These regions included the subscapular, waist, hip, and thigh regions. The regions were defined by anatomic bony landmarks. The height of each region was equivalent and was defined as one third the distance from the top of the iliac crest to the knee. The waist region was placed on the iliac crest, with the subscapular region placed on top of that. The hip region was placed at the middle of the pelvis, with the thigh region just below that. The width of each region was adjusted to include all soft tissue in that region. Body fat distribution was calculated as the fat mass in the subscapular region plus that in the waist region divided by the fat mass in the hip region plus that in the thigh region.

**Blood Pressure**

Blood pressure was measured in the right arm with the subject sitting quietly by use of the methodology described by the Second NHLBI Task Force on Blood Pressure Control in Children. Blood pressure was measured by trained examiners who had received 16 hours of instruction and were certified for blood pressure measurement as part of the quality control process for a multicenter investigation. Measurements were made by auscultation with a mercury-column sphygmomanometer and a cuff appropriately sized for the arm size of the subject. The onset of the first Korotkoff phase was used to determine systolic blood pressure, and the onset of the fifth Korotkoff phase was used to determine diastolic blood pressure. Three blood pressure measurements were taken. The average of the 3 measurements was used in the analysis.

**Lipids and Lipoproteins**

Blood was drawn from subjects after a 12-hour fast. Lipid profiles were measured in the Lipid Laboratory of the Department of Internal Medicine at the University of Cincinnati, which is an NHLBI-CDC-standardized laboratory. Analyses were performed on a Hitachi 705 analyzer with enzymatic procedures for measurement of cholesterol and triglycerides and triglyceride blanking, and the modified Lipid Research Clinic method was used for measurement of HDL cholesterol. The LDL cholesterol level was calculated by use of the Friedewald equation.

**Left Ventricular Mass**

Echocardiographic examination was performed with subjects in the supine position. Studies were performed with 2-dimensional guided M-mode echocardiography. Measurements of the left ventricle were made at end diastole according to the methods of the American Society of Echocardiography. Left ventricular mass was calculated as previously described. Left ventricular mass index was calculated as left ventricular mass (grams) divided by height (meters), as recommended by De Simone et al.

**Statistical Analysis**

Descriptive statistics, including mean and SD for continuous variables and proportions for categorical variables, were calculated. Appropriate transformations were performed for continuous variables that were not normally distributed. The dependent variables for this study were established cardiovascular risk factors, including lipid and lipoprotein concentrations, blood pressure, and left ventricular mass. Univariate relationships between body size variables and risk factors were assessed with correlation analysis. In these analyses, the values for lipids and lipoproteins were included after logarithmic transformation. To evaluate the independence of correlates of risk factor variables, stepwise multiple linear regression analysis was used. In these analyses, both the percent body fat and fat distribution were allowed to enter the model as independent variables. A value of $P<0.05$ indicated statistical significance.

**Results**

The study included 127 subjects: 68 were male and 59 were female; 72 were white and 55 were black. The mean ages were 11.9±2.6 years for white girls, 12.7±2.2 years for black girls, 13.4±1.5 years for white boys, and 13.5±1.6 years for black boys. Descriptive statistics for body fat measures and cardiovascular risk factors are presented in Table 1.

Univariate correlation coefficients between body fat measures and cardiovascular risk factors are presented in Table 2. Triglyceride concentration was related to body fat distribution, and HDL cholesterol was inversely associated with body fat distribution. Greater truncal fat distribution was associated with higher triglycerides and lower HDL cholesterol. HDL cholesterol was also inversely related to the total percent body fat and the amount of fat in the android segments. LDL cholesterol was not associated with any of the measures of body fat. Systolic blood pressure was related to both the total amount of fat and fat distribution, whereas diastolic blood pressure was related to the percent body fat but not fat distribution. Left ventricular mass was strongly correlated with both percent body fat and fat distribution.

Results of the multiple regression analysis for each of the dependent variables are presented in Table 3. Fat distribution was a significant independent predictor of both plasma triglyceride and HDL cholesterol levels. There was a direct relationship between the android/gynoid fat distribution and triglyceride concentration and an inverse relationship with plasma HDL cholesterol concentration. In these models, the fat distribution and age and fat distribution explained a relatively small but significant proportion of the variance of triglyceride and HDL cholesterol levels, respectively. An-
Variance of Cardiovascular Risk Factors

Table 2. Correlation Coefficients for Association Between Body Fat Measures and Cardiovascular Risk Factors

<table>
<thead>
<tr>
<th>Lipids and Lipoproteins</th>
<th>Blood Pressure</th>
<th>Left Ventricular Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Total Cholesterol</td>
<td>Log Triglycerides</td>
<td>Log HDL-C</td>
</tr>
<tr>
<td>Body mass index</td>
<td>−0.06</td>
<td>0.14</td>
</tr>
<tr>
<td>Percent body fat</td>
<td>−0.02</td>
<td>0.20†</td>
</tr>
<tr>
<td>Android region fat, kg</td>
<td>−0.09</td>
<td>0.15</td>
</tr>
<tr>
<td>Gynoid region fat, kg</td>
<td>−0.09</td>
<td>0.14</td>
</tr>
<tr>
<td>Fat distribution</td>
<td>0.02</td>
<td>0.27†</td>
</tr>
</tbody>
</table>

HDL-C indicates HDL cholesterol; LDL-C, LDL cholesterol. Left ventricular (LV) mass index=LV mass (g)/height (m)².7.

*P<0.05; †P<0.01; ‡P<0.001.

droid/gynoid fat distribution was also a significant correlate of systolic blood pressure and left ventricular mass. Fat distribution was not a significant predictor of diastolic blood pressure. In the multiple regression analyses, fat distribution was always a stronger correlate of the cardiovascular risk factors than percent body fat, which is an overall measure of obesity. Height was a significant independent correlate of systolic and diastolic blood pressures and left ventricular mass. Race was a correlate of diastolic blood pressure and left ventricular mass. The regression coefficient for race was negative in each model, indicating that blacks had higher diastolic blood pressure and left ventricular mass than whites. Sex was also a correlate of left ventricular mass, with boys having greater left ventricular mass than girls.

**Discussion**

We found that a greater android fat distribution was significantly and independently related to plasma triglycerides and HDL cholesterol, systolic blood pressure, and left ventricular mass. These results suggest that a relative preponderance of fat in the upper body, including abdominal fat, is an important determinant of cardiovascular risk factor status in children and adolescents. This is of particular importance because they may accumulate greater amounts of truncal fat and increasingly unfavorable cardiovascular risk status.

The association of increased body weight with elevated triglycerides and diminished HDL cholesterol has been described in both adults and children.17,18 These lipid and lipoprotein alterations have also been reported to be associated with measures of central obesity, such as waist-to-hip ratio in adults.19–21 Significant weight loss has been shown to result in decreased triglyceride and increased HDL cholesterol concentrations.22–23 The relationships between fat distribution and lipids and lipoproteins in the present study are similar to those found in adult subjects with the use of DEXA. Haarbo et al24,25 found positive associations between central fat and cholesterol, triglycerides, and LDL cholesterol and a negative association with HDL cholesterol in postmenopausal women. Walton et al10 studied healthy men 21 to 77 years of age and found a relationship of increasing android fat distribution and elevated serum triglycerides and decreased HDL C concentrations. They did not report an association between fat distribution and either LDL or HDL cholesterol. We found relationships of body fat distribution and triglycerides and HDL cholesterol in young subjects but did not find an association of fat distribution and LDL cholesterol.

From a clinical standpoint, there is often heterogeneity in the cardiovascular risk status in obese children and adolescents. In adults, the most typical lipid profile seen in obese individuals is increased fasting plasma triglyceride levels, reduced plasma HDL cholesterol, and marginally elevated plasma LDL cholesterol levels.26,27 In adult men and women, accumulation of abdominal fat is associated with high plasma triglyceride and low plasma HDL cholesterol levels.27

Previous studies in children have shown that there is a relationship between obesity and cardiovascular risk factors in populations of young subjects.28 We have previously shown the relationships between adiposity and blood pressure29,30 and left ventricular mass in children and adolescents.31 Some studies in young subjects have also evaluated the relationship of fat distribution and cardiovascular risk. These studies have generally supported the concept that fat distribution is related to cardiovascular risk factors.28 However, these studies have usually used less direct anthropometric measures, such as skin-fold thickness and waist and hip circumferences. These methods can be useful and convenient.
but are subject to variability because of differences in measurements or observer bias. DEXA has the advantage of direct measurement of fat and lean tissue mass and the ability to evaluate the differences in fat deposition by region. This allows more precise measurement of fat mass and a better understanding of the role of fat distribution.

The mechanism by which truncal fat deposition influences these cardiovascular risk factors is not completely understood. However, it is clear in adults that some metabolic alterations are related to more central fat deposition. Subjects with greater central fat have lower insulin sensitivity, resulting in higher circulating insulin levels and elevated concentration and turnover of nonesterified fatty acids.32 Visceral adipocytes are less responsive to the action of insulin in obesity states. This insulin resistance leads to increased delivery of fatty acids to the liver. These fatty acids are a determinant of triglyceride production in the liver.33 Elevated insulin concentrations may also influence the activity of hepatic lipase, and insulin resistance may affect lipoprotein lipase, both of which are involved in the metabolism of HDL cholesterol.34,35 Reduced lipoprotein lipase and increased hepatic lipase activity result in decreased maturation and increased catabolism of HDL cholesterol, respectively. Rocchini36 has studied the relationship of insulin sensitivity to blood pressure in obese adolescents and found that increased circulating levels of insulin are related to blood pressure elevation. This may be due to an effect of insulin on excretion of sodium and water, leading to increased circulating blood volume.37 Other possible mechanisms include an adverse effect of insulin on sympathetic nerve activity or on the endothelium.38 The effect of insulin on left ventricular mass may involve the growth-promoting action of insulin or other metabolic and hemodynamic effects of insulin.39

In conclusion, we found that the more android or more central fat distribution is an important predictor of plasma triglycerides, HDL cholesterol, systolic blood pressure, and left ventricular mass in children and adolescents. Fat distribution appears to be a more important influence on cardiovascular risk factors in young subjects than overall adiposity. These findings, for which a direct measure of fat distribution by region was used, indicate that understanding the impact of central adiposity on cardiovascular risk will be important in the design of future studies and planning of clinical intervention strategies to lower cardiovascular risk for young people.

References


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