Adipose Tissue Distribution and Plasma Lipoprotein Levels in Obese Women

Importance of Intra-abdominal Fat

Jean-Pierre Després, Sital Moorjani, Mario Ferland, Angelo Tremblay, Paul J. Lupien, André Nadeau, Sylvie Pinault, Germain Thériault, and Claude Bouchard

Prospective studies have shown that excess abdominal fat is associated with an increased risk of coronary heart disease and related death. We used computed axial tomography (CAT) to assess the association between deep and subcutaneous abdominal adipose tissue and plasma lipoprotein levels in a sample of 52 premenopausal obese women aged 35.7±5.5 years (mean±SD). Whereas the plasma lipoprotein concentrations were not significantly correlated with fat mass, the data obtained by CAT indicated that the absolute amount of deep abdominal fat was negatively correlated with high density lipoprotein cholesterol (HDL-CHOL) levels (r=-0.35, p<0.01), as well as with HDL-CHOL/LDL-CHOL, HDL- apo apo A-I/LDL- apo B, and HDL-Chol/HDL- apo B ratios (-0.32≤r≤-0.40, 0.05>p<0.01). Adipose tissue deposition at the mid-thigh region determined by CAT did not show any significant relationship with plasma lipoprotein levels. When subgroups of women with comparable ages and adiposity but with high and low intra-abdominal fat accumulation were compared, women with a high accumulation of intra-abdominal fat displayed significantly lower HDL-CHOL (p<0.001), HDL-Chol/LDL-CHOL (p<0.001), HDL-Chol/LDL-Chol (p<0.01), and HDL-apo A-I (p<0.05) levels, as well as reduced HDL-CHOL/LDL-CHOL (p<0.01), HDL-apo A-I/LDL-apo B (p<0.05), and HDL-Chol/HDL-Chol ratios (p<0.05) in comparison with obese women with low accumulations of intra-abdominal fat. These data indicate that, in a sample of obese women, body fat distribution, especially intra-abdominal fat accumulation, is a significant correlate of plasma lipoprotein levels independent of total fatness. (Arteriosclerosis 9:203-210, March/April 1989)

Several studies have shown the importance of adipose tissue distribution, in contrast to obesity, as a significant and independent cardiovascular risk factor. Indeed, recent longitudinal studies have indicated that excessive fat deposition in the trunk was associated with an increased incidence of coronary heart disease and related death. Subsequent findings have related excess trunk fat to numerous metabolic disturbances, such as glucose intolerance, hyperinsulinemia, diabetes, hypertension, and hypertriglyceridemia. Changes in plasma lipoprotein levels may also contribute to the cardiovascular disease risk that is associated with adipose tissue distribution, since low high density lipoprotein (HDL) cholesterol levels have been reported in subjects with excess abdominal fat. These studies have, however, generally used subcutaneous skinfold measurements and the waist-to-hip circumferences ratio (WHR) to estimate the proportion of abdominal fat.

It has been proposed that the intra-abdominal fat component could be of particular importance in the manifestation of metabolic perturbations that are associated with excess abdominal fat, since peripheral fat deposition is not associated with these metabolic disturbances. The only method that is presently available to measure noninvasively the amount of intra-abdominal fat is computed axial tomography (CAT). In a recent report, the amount of intra-abdominal fat measured by CAT was significantly correlated with plasma cholesterol and triglyceride levels in a sample consisting of both men and women. Although numerous studies have reported that the proportion of abdominal fat, as estimated by the WHR, was associated with changes in plasma triglyceride and lipoprotein-cholesterol concentrations, few studies have measured the potential relation of deep as well as subcutaneous fat to plasma lipoprotein levels. Therefore, further research on the potential associations between deep as well as subcutaneous fat and plasma lipoprotein and apoprotein (apo) levels appeared warranted. The present study reports on the relationships between adipose tissue distribution, including intra-abdominal fat and mid-thigh deposition of adipose tissue, and plasma lipoprotein levels. This work was supported by the Quebec Heart Foundation, the Canadian Fitness and Lifestyle Research Institute, NSERC of Canada, and by FRSQ-Quebec. Jean-Pierre Després is the recipient of a FRSQ scholarship, and Mario Ferland is the recipient of an NSERC fellowship. Address for correspondence: Jean-Pierre Després, Ph.D., Physical Activity Sciences Laboratory, PEPS, Laval University, Ste-Foy, Quebec, Canada G1K 7P4. Received March 10, 1988; revision accepted October 24, 1988.
pose tissue measured by CAT, and plasma lipoprotein levels in a sample of 52 premenopausal obese women. Our results emphasize the importance of intra-abdominal fat and the negligible effect of thigh fat in the association between body fat distribution and plasma lipoproteins.

Methods

Subjects

Fifty-two premenopausal obese women were recruited by solicitation through the media. All subjects signed an informed document approved by the Laval University Medical Ethics Committee. A complete physical examination, which included medical history, was performed by a physician. Women with cardiovascular disease or endocrine disorders or those on medication were excluded. A glucose tolerance test was performed, and diabetic subjects were excluded from the study. All measurements were performed while the subjects were in the follicular phase of their menstrual cycle and in an apparent weight-stable period.

Computed Axial Tomography

CAT was performed on a Siemens Somatom DRH scanner (Erlangen, FRG) using the procedures described by Sjöström et al. The scanning was performed with 125 kV and a slice thickness of 8 mm. Briefly, the subjects were examined in the supine position with their arms stretched above their heads. Three CAT scans were performed, and a radiograph of the skeleton was used as a reference to establish the position of the scans at the nearest millimeter: Th8 to Th9, L4 to L5, and mid-thigh. The total and deep fat areas were calculated by delineating these areas with a graph pen and then computing the adipose tissue surfaces with an attenuation range of -30 to -190 HU. The intra-abdominal fat area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The subcutaneous fat was calculated by subtracting the amount of intra-abdominal fat from the total fat area. The distance between adjacent scans was also measured, and the adipose tissue volume between these scans was calculated. The average of mid-thigh and abdominal scan areas was multiplied by the distance between these two adjacent scans, and this partial adipose tissue volume added up to the volume of adipose tissue calculated from the abdominal scan to the thoracic scan. These two partial volumes were, therefore, considered as two different cylinders. The assumption underlying this procedure is that there is a linear change in adipose tissue measured by CAT, and plasma lipoprotein levels in a sample of 52 premenopausal obese women. Our results emphasize the importance of intra-abdominal fat and the negligible effect of thigh fat in the association between body fat distribution and plasma lipoproteins.

Measurement of Body Fatness

Body density was measured by the hydrostatic weighing technique as previously described. The mean of six valid measurements was used in the calculation of percent body fat from body density using the equation of Siri. Fat mass was obtained by multiplying the percent of body fat by body weight. Pulmonary residual volume was measured using the helium dilution method of Meneely and Kaltreider.

Waist and hip circumferences were measured by the procedures of the Airlie Conference. The circumference measurements were performed while the women were wearing light underwear. The women stood erect with the abdomen relaxed. An inelastic tape was placed around each woman in a horizontal plane at the level of the natural waist, that is, the narrowest part of the torso. When this location was not easily found, the smallest horizontal circumference between the ribs and the iliac crest was measured to the nearest 0.1 cm. For the measurement of hip circumference, the measurement was performed at the side of the subject so that the level of maximum extension of the buttocks could be seen. An inelastic tape was placed around the buttocks in a horizontal plane. The maximum circumference at this level was measured to the nearest 0.1 cm.

Concomitant Lifestyle and Biologic Variables

Because of their potential association with plasma lipoprotein-cholesterol and apoprotein values, the effects of several concomitant variables: age; maximal oxygen consumption; daily energy intake; percentage of intake from proteins, lipids, and carbohydrates; and alcohol consumption were studied. There were too few smokers in the sample to study the effect of smoking.

Maximal oxygen consumption (VO2 max) was assessed on a progressive test to exhaustion on a treadmill. VO2 was recorded with an open gas circuit system, and VO2 max was considered to be the highest VO2 recorded during the test for 1 minute. Mean daily energy intake was determined with a 3-day dietary record including one weekend day as previously described. The tables of Dubuc and Lahalle were used to determine energy intake and percentage of energy derived from proteins, lipids, and carbohydrates. Alcohol consumption was reported in the 3-day dietary record and was calculated in grams of alcohol per day.

Plasma Lipoprotein and Apoprotein Analyses

Blood samples were collected from an antecubital vein into Vacutainer tubes (Becton Dickinson Labware) containing EDTA. Samples were taken in the morning after a 12-hour fast while the subjects were in a supine position. Blood sampling was done in the early follicular phase. Cholesterol (CHOL) and triglyceride (TG) levels were determined in plasma and lipoprotein fractions after extraction with isopropanol and treatment with zeolite according to the Technicon AA-II procedure. Plasma very low density lipoproteins (VLDL, d<1.006 g/ml) were isolated by ultracentrifugation, and the HDL fraction was obtained after precipitation of low density lipoprotein (LDL) in the infranatant (d>1.006 g/ml) with heparin and MnC12. The CHOL and TG contents of the infranatant fraction were measured before and after the precipitation step. Apo B concentration was measured in plasma and in the infranatant (LDL- apo B) by the rocket immu-no-electrophoretic method of Laurell as previously described. Apo A-I concentration was also measured in the infranatant frac-
The sample included 52 obese women; the controls were 25 nonobese women matched for age. BMI = body mass index, CHOL = cholesterol, TG = triglyceride, HDL = high density lipoprotein.

<table>
<thead>
<tr>
<th>Table 1. Physical Characteristics and Plasma Lipid Levels in Obese Women Compared with Nonobese Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Body fat (%)</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
</tr>
<tr>
<td>Plasma CHOL</td>
</tr>
<tr>
<td>Plasma TG</td>
</tr>
<tr>
<td>Plasma HDL-CHOL</td>
</tr>
</tbody>
</table>

Values are means±SD. *p<0.001, †p<0.0001.

Statistical Analyses

Relationships between variables were measured by Pearson’s product-moment correlation coefficients. The associations between adipose tissue distribution and plasma lipoprotein levels were further studied by comparing two subgroups of ten subjects each with the highest and the lowest WHR values. Differences between these two subgroups were tested for statistical significance using Student’s t test. Data on the plasma TG, as well as VLDL components, were log-transformed to normalize their distribution. Multivariate analyses were also performed to evaluate the variance in lipoprotein-cholesterol and apoprotein levels that could be explained by the body fatness, body fat distribution, and concomitant variables. Only variables that displayed significant univariate correlations with the dependent lipoprotein variables were included in the stepwise multiple regression procedure in which all possible permutations of relevant independent variables were tested. The Statistical Analysis System was used to perform these analyses.

Results

The physical characteristics and the plasma lipid and HDL-CHOL levels of obese women are presented in Table 1. Their values are compared with those from a sample of 25 nonobese women who were studied for other research purposes but for whom we had adiposity, plasma lipid, and HDL-CHOL measurements taken by the same methods as for the obese women. In addition to having higher adiposity than nonobese women, obese women had significantly higher plasma CHOL and TG, and lower HDL-CHOL levels (p<0.001). The body mass index (BMI) of obese women ranged from 25.6 to 46.5 kg/m², and their body density measurements confirmed that women had significantly higher plasma CHOL and TG, and their body density measurements confirmed that the HDL-CHOL/HDL-TG ratio (r=-0.45, p<0.001), suggesting apoprotein enrichment of LDL particles. In addition, WHR was negatively correlated with the HDL-CHOL/LDL-CHOL ratio (r=-0.44†, p<0.001). However, the proportion of abdominal fat, as measured by WHR, was negatively correlated with lipoprotein indices of coronary heart disease (HDL-CHOL/LDL-CHOL, HDL₃-CHOL, and HDL-apo A-I levels. Various lipoprotein ratios were calculated to estimate the coronary heart disease risk associated with total adiposity and fat distribution. Total fat mass was not correlated with any of these ratios, whereas BMI was negatively correlated with the HDL-CHOL/LDL-CHOL ratio (p<0.05). However, the proportion of abdominal fat, as measured by WHR, was negatively correlated with lipoprotein indices of coronary heart disease (HDL-CHOL/LDL-CHOL, HDL₃-CHOL, and HDL-apo A-I levels. In addition, WHR was negatively correlated with the HDL-CHOL/LDL-CHOL ratio (r=-0.45, p<0.001), suggesting an enrichment of the HDL particle with TG in subjects with excess abdominal fat. Such enrichment was not observed in the LDL fraction (results not shown).

There was, however, a positive correlation between WHR and the ratios of LDL-apo B/LDL-CHOL (r=0.35, p<0.05) indicating apoprotein enrichment of LDL particles.

The absolute and relative amounts of intra-abdominal fat measured by CAT were significantly correlated with WHR (r=0.50 and 0.46, respectively, p<0.001). The amount of subcutaneous abdominal fat measured at the L4 to L5 region was not correlated with plasma lipoprotein levels (Table 3). The amount of deep abdominal fat, however, was negatively correlated with plasma HDL-CHOL levels (r=-0.35, p<0.01). Deep abdominal fat...
were observed between the two subgroups. Women with high WHR values did not show higher levels of subcutaneous abdominal adipose tissue than did subjects with low WHR, but they had significantly more deep adipose tissue at the abdominal region (L4 to L5) than did women with low WHR (p<0.001). This higher amount of deep abdominal fat in subjects with high WHR was noted whether the deep adipose tissue deposition was expressed in absolute (cm²) or relative (deep abdominal fat area/total abdominal fat area) values. Women with high WHR also had comparable adipose tissue areas at the mid-thigh level compared with women with low WHR. Women with high WHR, however, had a higher ratio of abdominal to mid-thigh fat areas compared with women with low WHR (p<0.05).

To further study the associations between fat distribution and plasma lipoprotein levels, subgroups of obese women with the highest and lowest WHR were compared (Table 4). No differences in age and in percent body fat were observed between the two subgroups. Women with high WHR values did not show higher levels of subcutaneous abdominal adipose tissue than did subjects with low WHR, but they had significantly more deep adipose tissue at the abdominal region (L4 to L5) than did women with low WHR (p<0.001). This higher amount of deep abdominal fat in subjects with high WHR was noted whether the deep adipose tissue area was expressed in absolute (cm²) or relative (deep abdominal fat area/total abdominal fat area) values. Women with high WHR also had comparable adipose tissue areas at the mid-thigh level compared with women with low WHR. Women with high WHR, however, had a higher ratio of abdominal to mid-thigh fat areas compared with women with low WHR (p<0.05).

Women with high WHR had lower levels of HDL-CHOL (p<0.001) as well as reduced HDL₂-CHOL and HDL₃-CHOL levels (p<0.01) (Table 5). A significant reduction in plasma HDL-apo A-I was also observed in women with high intra-abdominal fat deposition compared with women with low levels of intra-abdominal fat (p<0.05). Trends for

### Table 3. Correlation Coefficients between Adipose Tissue Volume Determined by Computed Axial Tomography, Adipose Tissue Areas at the L4 to L5 Region, and Plasma Lipoproteins In Obese Women

<table>
<thead>
<tr>
<th>Adipose tissue volume</th>
<th>Abdominal scan areas</th>
<th>Total</th>
<th>Deep</th>
<th>Subc</th>
<th>Deep/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLDL-CHOL (log 10)</td>
<td>0.10</td>
<td>0.06</td>
<td>0.20</td>
<td>0.02</td>
<td>0.24</td>
</tr>
<tr>
<td>VLDL-TG (log 10)</td>
<td>0.13</td>
<td>0.12</td>
<td>0.24</td>
<td>0.06</td>
<td>0.24</td>
</tr>
<tr>
<td>VLDL-apo B (log 10)</td>
<td>-0.11</td>
<td>-0.23</td>
<td>-0.15</td>
<td>-0.22</td>
<td>0.00</td>
</tr>
<tr>
<td>LDL-CHOL</td>
<td>0.14</td>
<td>0.13</td>
<td>0.23</td>
<td>0.07</td>
<td>0.23</td>
</tr>
<tr>
<td>LDL-TG</td>
<td>0.07</td>
<td>0.09</td>
<td>0.13</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td>LDL-apo B</td>
<td>0.16</td>
<td>0.17</td>
<td>0.26</td>
<td>0.11</td>
<td>0.22</td>
</tr>
<tr>
<td>HDL-CHOL</td>
<td>-0.29*</td>
<td>-0.29*</td>
<td>-0.35</td>
<td>-0.22</td>
<td>-0.24</td>
</tr>
<tr>
<td>HDL-TG</td>
<td>-0.04</td>
<td>-0.07</td>
<td>0.07</td>
<td>-0.11</td>
<td>0.13</td>
</tr>
<tr>
<td>HDL-apo A-I</td>
<td>-0.30*</td>
<td>-0.27</td>
<td>-0.28</td>
<td>-0.23</td>
<td>-0.18</td>
</tr>
<tr>
<td>HDL₂-CHOL</td>
<td>-0.31*</td>
<td>-0.29*</td>
<td>-0.37</td>
<td>-0.22</td>
<td>-0.26</td>
</tr>
<tr>
<td>HDL₃-CHOL</td>
<td>-0.20</td>
<td>-0.22</td>
<td>-0.27</td>
<td>-0.17</td>
<td>-0.15</td>
</tr>
<tr>
<td>HDL-CHOL/LDL-CHOL</td>
<td>-0.29*</td>
<td>-0.28*</td>
<td>-0.40*</td>
<td>-0.19</td>
<td>-0.36*</td>
</tr>
<tr>
<td>HDL₂/A-I/ VLDL-B</td>
<td>-0.26</td>
<td>-0.25</td>
<td>-0.37</td>
<td>0.16</td>
<td>-0.35*</td>
</tr>
<tr>
<td>HDL₂/CHOL/HDL₃/CHOL</td>
<td>-0.28*</td>
<td>-0.24</td>
<td>-0.32</td>
<td>-0.17</td>
<td>-0.26</td>
</tr>
</tbody>
</table>

Subc=subcutaneous, VLDL=very low density lipoprotein, LDL=low density lipoprotein, HDL=high density lipoprotein, CHOL=cholesterol, TG=triglyceride, apo=apolipoprotein.

### Table 4. Adiposity and Computed Tomography-derived Measurements of Adipose Tissue Distribution In Obese Subjects with Lowest and Highest Values of Waist-to-Hip Circumference Ratio

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low WHR</th>
<th>High WHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>36.0±4.0</td>
<td>36.1±2.8</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>47.0±6.4</td>
<td>49.8±3.2</td>
</tr>
<tr>
<td>WHR</td>
<td>0.74±0.04</td>
<td>0.89±0.02</td>
</tr>
<tr>
<td>L4 to L5 total (cm²)</td>
<td>658.8±118.0</td>
<td>802.0±153.8*</td>
</tr>
<tr>
<td>L4 to L5 subc (cm²)</td>
<td>551.8±94.7</td>
<td>615.3±141.0</td>
</tr>
<tr>
<td>L4 to L5 deep (cm²)</td>
<td>107.0±33.4</td>
<td>186.7±36.9*</td>
</tr>
<tr>
<td>L4 to L5 deep/tot</td>
<td>0.16±0.04</td>
<td>0.24±0.05</td>
</tr>
<tr>
<td>L4 to L5 total/mid-thigh</td>
<td>1.29±0.23</td>
<td>1.53±0.19*</td>
</tr>
<tr>
<td>Mid-thigh total (cm²)</td>
<td>517.5±93.4</td>
<td>527.9±94.9</td>
</tr>
</tbody>
</table>

There were 10 women in each group. WHR=waist-to-hip ratio, L4 to L5=abdominal scan, Subc=subcutaneous. Values are means±SD.  
*0.05<p<0.06, †p<0.05, ‡p<0.01.
The WHR was better than deep abdominal fat as an independent covariate of HDL-CHOL, LDL-Chol, and HDL-apo A-I levels. The only other independent variable that contributed significantly to the variance of HDL was alcohol intake for HDL-CHOL (6.3% of the variance) and HDL-apo A-I (11.6% of the variance). Deep abdominal fat, however, displayed significant associations with lipoprotein ratios (HDL-CHOL/LDL-Chol, HDL-apo A-I/LDL-apo B, and HDL2-Chol/HDL3-Chol) that were independent of all other variables.

Furthermore, after deep abdominal fat was entered into the regression procedure, no other adiposity or concomitant variable could explain further the variance of these three lipoprotein ratios.

Discussion

Although recent prospective studies have shown that body fat distribution is significantly associated with cardiovascular disease, the mechanisms for this association remain to be discovered. Since the early works of Vague, numerous reports have shown that adipose tissue topography is associated with cardiovascular risk factors such as glucose intolerance, insulin resistance, hypertension, and changes in plasma lipid concentrations. The link between body fat distribution and these risk factors is considered as one of the metabolic mechanisms by which body fat topography is associated with cardiovascular disease. High levels of abdominal fat have been associated with elevated plasma TG concentrations and low HDL-Chol levels, and these associations, which have been shown to be independent of the effect of obesity, could also help explain the association between regional body fat distribution and cardiovascular disease.

In the present sample of obese women, we found little association between total fatness and plasma lipoprotein levels. Such a lack of relationship could be due to the nature of the sample, since all our subjects were obese. Indeed, when the plasma lipid levels of our obese patients were compared with those measured in lean women of similar ages, significant differences were observed between the two groups, indicating (in concordance with the results of numerous studies) that obesity is associated with increased levels of plasma lipids. The present study suggested, however, that in a sample of obese women in which little association between total fatness and plasma lipoprotein levels is found, adipose tissue distribution is a significant correlate of plasma lipoprotein concentrations.

The concentration and composition of HDL showed significant associations with fat distribution. In concordance with other studies, WHR displayed a significant association with plasma HDL-Chol levels, whereas HDL-apo A-I levels were not an independent correlate of plasma lipoprotein levels. The WHR was the only independent variable associated with the variance of plasma VLDL-Chol and VLDL-TG levels. No independent variable could significantly account for the variance in LDL-Chol, LDL-TG, and LDL-apo B concentrations. Therefore, VLDL and LDL results are not included in Table 6.
tively correlated with WHR, suggesting an increased risk of cardiovascular disease in women with high levels of abdominal fat. Apo A-1 and B measurements are also commonly used in the estimation of cardiovascular disease risk because they provide estimates of HDL and LDL particle number, respectively. Whereas total fat mass was not correlated with HDL-apo A-1/LDL-apo B ratio, the WHR was \( r = -0.33 \) (\( p < 0.05 \)), indicating that obese subjects with a high proportion of abdominal fat also had a reduced ratio of HDL to LDL particles, which could add to their susceptibility to atherosclerosis. The lack of any significant association between total fatness and these ratios should, however, be interpreted with caution because all our women were obese. In a random sample including obese and nonobese subjects, significant associations between obesity and some of these atherogenic indices have been found.

Because WHR provides only an anthropometric estimate of the proportion of abdominal fat, we used CAT to further study the association between deep and subcutaneous abdominal fat deposition and plasma lipoprotein levels. The only study that has used this approach to measure intra-abdominal fat reported significant associations between the visceral/subcutaneous abdominal fat ratio and plasma TG and CHOL levels in a sample of 46 subjects, 15 men and 31 women, including 12 diabetic subjects. Our data in premenopausal obese women showed that the intra-abdominal fat area measured at the L4 to L5 region was negatively correlated with plasma HDL-CHOL, HDL2-CHOL, HDL-apo A-1, and with lipoprotein ratios used in the prediction of the cardiovascular disease risk.

A high deposition of fat in the thigh region was not, however, associated with any change in the concentration of plasma lipoproteins. These results on peripheral fat measured by CAT are concordant with previous observations that indicated that peripheral accumulation of body fat, as observed in gynoid obesity, is not associated with metabolic complications and, therefore, does not represent a major health hazard.

These results further support the concept that the rather moderate association that is consistently found between obesity and cardiovascular disease could be due, at least partly, to the fact that obese subjects are metabolically heterogeneous and that an alteration in body fat distribution is the critical variable in detecting the obesity-related metabolic complications. Our findings in obese women with extreme WHR values further emphasize this point. Although the subgroup of obese women with the lowest WHR had almost 50% of their body weight as fat, they did not show substantial elevations in their plasma CHOL and TG concentrations. In contrast, women with high WHR of similar age and relative adiposity, but showing greater absolute and relative amount of deep fat at the abdominal region, displayed a lipoprotein profile that is associated with an increased risk of cardiovascular disease. In comparison with the obese women with low WHR, obese women with high WHR had reduced plasma HDL-CHOL, HDL2-CHOL, and HDL-apo A-1 levels, and reduced ratios of HDL2-CHOL/HDL-CHOL, HDL-ChOL/LDL-ChOL, as well as a reduced HDL-apo A-1/LDL-apo B ratio, indicative of an increased cardiovascular disease risk. The data on these subgroups of obese women with similar body composition, but differing only in their amount of intra-abdominal fat, further emphasize the importance of deep abdominal fat as a significant covariate of plasma lipoprotein levels in obese subjects.

Results from our multivariate analyses, which included concomitant variables such as age, energy intake, proportion of intake as proteins, lipids and carbohydrates, alcohol intake, and VO2 max indicated that intra-abdominal fat accumulation displayed significant associations with lipoprotein ratios (HDL-CHOL/LDL-CHOL, HDL-apo A-1/LDL-apo B, HDL2-CHOL/HDL2-CHOL) that were independent from all other variables studied. Indeed, no other variable could account for a significant portion of the variance of these ratios after intra-abdominal fat had been entered into the regression models. WHR was, however, better than deep abdominal fat as an independent covariate of HDL-CHOL, HDL2-CHOL, and HDL-apo A-1. Therefore, from a practical standpoint, it could be argued that an inexpensive WHR can be used to assess the proportion of

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Table 6. Stepwise Regression Analyses for Relative Contributions of Body Fat, Fat Distribution, and Lifestyle Variables to Variance of High Density Lipoproteins and Lipoprotein Ratios in Obese Women

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable(s) (partial ( r^2 ))</th>
<th>Total ( r^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-CHOL</td>
<td>WHR (22.4%) + alcohol (6.3%)</td>
<td>28.7%</td>
</tr>
<tr>
<td>HDL2-CHOL</td>
<td>WHR (18.3%)</td>
<td>18.3%</td>
</tr>
<tr>
<td>HDL-apo A-1</td>
<td>Alcohol (11.6%) + WHR (9.9%)</td>
<td>21.5%</td>
</tr>
<tr>
<td>HDL-CHOL/LDL-CHOL</td>
<td>L4 to L5 deep fat (16.9%)</td>
<td>16.9%</td>
</tr>
<tr>
<td>HDL-apo A-1/LDL-apo B</td>
<td>L4 to L5 deep fat (14.6%)</td>
<td>14.6%</td>
</tr>
<tr>
<td>HDL-CHOL/HDL2-CHOL</td>
<td>L4 to L5 deep fat (10.0%)</td>
<td>10.0%</td>
</tr>
</tbody>
</table>

The waist-to-hip ratio (WHR) was the only independent variable that was significantly associated with plasma TG and LDL levels (see Table 2). LDL-CHOL, LDL-TG, and LDL-apo B levels were not significantly correlated with body fat or with body fat distribution in this sample. Only the independent variables that displayed significant univariate correlations with the dependent lipoprotein variables were entered in the stepwise analyses, and all possible permutations of variables were tested.

L4 to L5 = Abdominal scan, HDL = high density lipoprotein, CHOL = cholesterol, apo = apolipoprotein.

See the legend to Table 2 for abbreviations.
abdominal fat instead of measuring deep abdominal fat by an expensive CAT technique. From a physiological point of view, however, the results of the present study suggest that deep abdominal fat is probably the important body fat distribution variable because it is an independent covariate of the lipoprotein ratios considered important in estimating cardiovascular disease risk. The results from multivariate analyses indicate that WHR does not always "capture" the relation of deep abdominal fat to plasma lipoproteins. Therefore, in epidemiological studies, WHR is probably the best anthropometric estimator of deep abdominal fat accumulation available. In metabolic studies, however, it appears important to directly measure intra-abdominal fat accumulation to further understand the mechanisms involved in the association between body fat distribution and metabolic complications.

It has been suggested that the high plasma VLDL levels associated with excess abdominal fat may be secondary to an increased free fatty acid (FFA) flux from the omental adipocytes to the liver. Such a condition has also been associated with a reduced hepatic extraction of insulin. The resulting peripheral hyperinsulinemia combined with high plasma FFA levels would induce an increased hepatic VLDL secretion. The positive correlation observed between WHR and the ratio of apo A-I/CHOL in the HDL fraction suggests a cholesterol depletion of HDL particles associated with excess abdominal fat and an enrichment of HDL with triglycerides, a phenomenon that has been reported in subjects with high plasma triglyceride levels. Because glucose intolerance and hyperinsulinemia are conditions associated with abdominal obesity, we performed preliminary analyses that indicated that alterations in carbohydrate metabolism could not account for much of the variance in plasma lipoprotein levels associated with deep abdominal fat accumulation (results not shown). Although further research is needed to address this issue, these preliminary data suggest that additional mechanisms may be operative in the body fat distribution/plasma lipoproteins association.

It has been shown that human fat cells can interact specifically and satura[href]ly with HDL. The fat cell-HDL metabolism displays regional variation, and a positive correlation has been reported between abdominal fat cell size and the level of apolipoprotein HDL binding. Because of the selective uptake of HDL cholesterol ester by human fat cells, the increased fat cell/HDL interaction observed in abdominal obesity could be another factor explaining the negative association between the amount of abdominal fat and plasma HDL cholesterol concentration.

In summary, the present study suggests that the altered lipoprotein profile associated with an excessive deposition of intra-abdominal fat should be considered as an important variable in the assessment of the cardiovascular disease risk of obese women. Further research is clearly warranted to identify the mechanisms responsible for this association and to verify whether this covariation represents a cause-effect relationship.

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