A Comparison of Abdominal Subcutaneous Adipose Tissue Pattern in Obese and Lean HIV-Infected Women

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ABSTRACT Cells from the superficial and deep subcompartments of the abdominal subcutaneous adipose tissue (SAT) compartment have distinct metabolic activities in vitro. The effect of differing energy balance on the relative in vivo sizes of these subcompartments has not been reported. We retrospectively investigated the effects of obesity and leanness on the relative amounts of superficial and deep SAT in the bulky posterior abdominal adipose tissue in HIV+ women. We studied the baseline results of MRI scans in 32 obese and 28 lean HIV-infected women. We also compared the change in response to specific interventions. Abdominal MRI slices were obtained at the L4-L5 and L2-L3 intervertebral spaces and were divided into anterior and posterior halves. The posterior portions were further subdivided into deep (PDSAT) and superficial layers (PSSAT) based on tissue planes visible on the MRI. Fat areas in adjacent landmark levels at the trochanter and anterior superior iliac spine were also obtained. PDSAT was larger at L4-L5 than at L2-L3 in both the lean and obese groups. PDSAT was larger than PSSAT at L4-L5 in obese women, and there was preferential loss of PDSAT in obese women who completed a 12-wk energy-deficit diet and exercise program. The contents of PDSAT and PSSAT did not differ in the lean group, and proportional increases in both SAT subcompartments were noted in response to weight gain. In summary, obesity is associated with a preferential increase in PDSAT and greater loss in PDSAT after weight loss. This study defines distinct metabolism responses in fat subcompartments. J. Nutr. 135: 53–57, 2005.

KEY WORDS: • obesity • subcutaneous adipose tissue • diet and exercise • magnetic resonance imaging • body composition

Although the role of obesity in promoting type 2 diabetes and cardiovascular risk is well recognized, increasing evidence implicates fat distribution as an additional risk factor (1). Abdominal adiposity is independently associated with cardiovascular risk, in addition to total body adiposity (2,3). Many studies showed that intra-abdominal, visceral adipose tissue (VAT) is strongly associated with cardiovascular risk, and that reduction in VAT improves the metabolic profile, notably insulin resistance and dyslipidemia (4). The role of abdominal subcutaneous adipose tissue (SAT) in relation to insulin resistance is less well recognized (5). Nevertheless, some cross-sectional studies suggested that subcompartments of SAT may have differential associations with insulin resistance (6,7).

The development of imaging methodologies has allowed the abdominal SAT subcompartments to be quantified in vivo. Previous studies suggested that the different subcompartments have distinct metabolic activities. For example, the results of in vitro studies show that, upon isoproterenol stimulation, adipocytes from deep abdominal SAT have higher lipolytic rates than adipocytes from the superficial compartment, in both humans and animals (8,9). Although in vivo signals and the pathways regulating lipid metabolism are more complex than those in a controlled in vitro study, a difference in metabolism in the 2 compartments could lead to different rates of gain and loss due to changes in energy intake or other factors.

Kelley et al. (7) reported that abdominal SAT is not evenly distributed around the circumference of the abdomen, in that the thickness of the adipose tissue layer is greater posteriorly than anteriorly. In addition, the abdominal posterior deep SAT (PDSAT) accounted for the majority of posterior SAT in obese women. The relative amounts of superficial and deep subcutaneous fat in lean states have not been reported.

The estimation of superficial and deep SAT is further complicated by the fact that the relations are not constant over the abdomen (Fig. 1). The phenomenon appears to be much more apparent in obese subjects than in lean subjects. This distribution disparity, if true, suggests that the superficial and deep posterior SAT subcompartments have either different rates of fat deposition, lipolysis, or both.

We tested the hypothesis that PDSAT and PSSAT respond differently to alterations in energy balance by comparing their relative contents among obese and lean HIV-infected women. We also examined the effects of weight gain in the lean

1 Supported by the National Institutes of Health (NIDDK 42618) and Serono, Incorporated.
2 To whom correspondence should be addressed. E-mail: dpkotler@aol.com.
3 Abbreviations used: ANCOVA, analysis of covariance; ASIS, anterior superior iliac spine; CT, computed tomography; PDSAT, posterior deep subcutaneous adipose tissue; PSSAT, posterior superficial subcutaneous adipose tissue; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.
women and weight loss in the obese women by a retrospective examination of the results of 2 completed clinical studies (10).

MATERIALS AND METHODS

Subjects. Baseline and longitudinal data from 2 clinical trials were analyzed retrospectively. Baseline body composition results from 32 HIV-infected women recruited for a diet and exercise study were examined. The women were obese with a BMI > 30 kg/m² at the time of enrollment (in year 2000). No subjects had reported drastic

weight change before enrollment into the parent study. The subjects were clinically stable and had no evidence of AIDS or lipodystrophy. Only one subject reported a history of illicit drug usage and was in the process of rehabilitation. The program consisted of 12 wk of consuming a low-energy diet (1200 kcal/d, 1 kcal = 4.184 kJ) and supervised aerobic and resistance exercise 3 times per week; 17 of 18 women who completed the program were restudied.

Baseline body composition results from another group of 28 women, who had participated in a study comparing the effects of a 12-wk program of a whey protein supplement, resistance exercise, or combined protein and exercise treatment on body composition, also were analyzed. These malnourished, lean subjects were HIV⁻ and had a body cell mass < 90% of gender and race-adjusted normal values (enrolled in year 1997–1998). The study protocol included a 6-wk weight stabilization period before study intervention. The results in 26 subjects who completed the study also were analyzed. The parent studies were approved by the Institutional Review Board at St. Luke’s-Roosevelt Hospital Center and all subjects gave informed consent.

MRI scanning. A single MRI protocol was applied to scan all subjects in both studies. The protocol, described previously (11), generates ~42 slices of MRI images depending on the subject’s height. The current study concentrated on subcompartments of SAT in the abdomen. The superficial fascia in the abdominal wall is usually divided into 2 layers, the superficial layer (Campe’s fasciae) and the deep layer (Scarpa’s fascia), especially when abdominal obesity is present (12). The boundary plane between the 2 layers is a condensate membrane-like fibrous network, which facilitates its recognition with imaging methodology such as computerized tomography (CT) or MRI. The fibrous network appears as a line with higher density than adipose tissue on a CT image and as a lower signal band than its surrounding fat on a T1-weighted MRI image. Accordingly, abdominal SAT can be separated unambiguously into 2 subcompartments, superficial and deep (13).

All MRI images were analyzed by the same analyst using research software (SliceOmatic, Version 4.0, Tomovision) to determine whole-body SAT volume as well as SAT areas at the levels of the greater trochanter of femur, anterior superior iliac spine, L4-L5 intervertebral space, and the L2-L3 intervertebral space. The abdomen at L4-L5 and L2-L3 was first divided into posterior and anterior halves by a line drawn in a coronal plane midway between the anterior and posterior surfaces. Posterior SAT was further subdivided into PDSAT and PSSAT after visually locating the separating line between the 2 layers.

Data analysis. Total body SAT volumes were calculated as described previously (11) and expressed in liters (L); SAT areas of individual MRI image slices at the above-mentioned levels are expressed in cm². Our sample conformed to normal distribution, and the probabilities from goodness-of-fit tests for normal distribution were >0.15 for both adipose tissue compartments in each group. Paired t tests were used to compare relative amounts of PDSAT and PSSAT at various levels within each group and Student’s t tests with uneven variant were used to compare counterparts in the lean and obese groups. A simple linear correlation model was used to determine possible relations among various subcompartments. Analysis of covariance (ANCOVA) was used to determine whether the relation within group was actually group-specific. Step-wise multiple regression models were used to determine predictors of PDSAT at L45. All analysis was performed with SAS software (Version 8, SAS Institute). The significance level was set at P < 0.05.

RESULTS

There was a clear distinction of general and specific fat distribution patterns between lean and obese women (Table 1). There were 22 African-American, 6 Hispanic, and 3 Caucasian women in the obese group; the ethnicity of 1 woman was not determined. There were 21 African-American, 2 Caucasian, and 5 Hispanic women in the lean group. The 2 groups did not differ in age (P = 0.71). BMI, total body SAT, and SAT at the greater trochanter of the femur, the superior iliac spine, and the L4-L5 and L2-L3 intervertebral spaces
TABLE 1

Demographic characteristics and SAT areas at different anatomic levels in lean and obese HIV-infected women

<table>
<thead>
<tr>
<th></th>
<th>Obese group</th>
<th>Lean group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td>Age, y</td>
<td>40.7 ± 7.1</td>
<td>39.9 ± 9.0</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>34.5 ± 3.4</td>
<td>22.3 ± 2.2*</td>
</tr>
<tr>
<td>Total body SAT, L</td>
<td>43.2 ± 1.7</td>
<td>18.3 ± 1.8*</td>
</tr>
</tbody>
</table>

1 Values are means ± SD. * Different from the obese group, $P < 0.001$.

were larger in the obese group compared with the lean group (all $P < 0.001$).

Within the obese group, PDSAT was larger than PSSAT ($P < 0.001$) at the L4-L5 level by paired $t$ test. There was no simple correlation between PDSAT and PSSAT areas ($r = 0.23, P = 0.19$). Total SAT, posterior SAT, and PDSAT at L4-L5 were significantly larger than those at L2-L3 by paired $t$ tests. In contrast, the areas of PSSAT at L4-L5 and at L2-L3 did not differ ($P = 0.16$). The VAT areas were 118.9 ± 7.8 and 123.7 ± 9.9 cm² at L4-L5 and L2-L3, respectively; there was no difference in VAT between the 2 segments, whereas the ratio of VAT over SAT at these 2 segments differed ($P < 0.001$).

Within the lean group, PDSAT and PSSAT did not differ at the L4-L5 level. In addition, there was a significant simple correlation between PDSAT and PSSAT ($r = 0.68, P < 0.001$) at the same level. Total SAT, posterior SAT, PDSAT, and PSSAT at L4-L5 all were significantly larger than the contents at L2-L3 by paired $t$ tests.

In each group, there was an association between total body SAT and PDSAT at L4-L5 (Fig. 2). To determine whether the associations were group specific, ANCOVA was performed with total body SAT as a covariate, PDSAT as a dependent variable, and group as a class variable. In this model, the group variable was significant ($P = 0.034$).

Stepwise multiple regression in the 2 groups showed that total SAT at the L2-L3 intervertebral space was strongly associated with PDSAT at the L4-L5 intervertebral space in both the obese (Table 2) and lean groups (Table 3). Neither race nor age was a significant variable in the model.

In the 17 obese women who completed the 12-wk energy-deficit diet and exercise program, total body SAT fell by 6.2 L ($44.7 ± 10.4$ to $38.5 ± 10.3$ L, $P < 0.0001$), total body VAT decreased by 20% from $3.9 ± 1.2$ to $3.2 ± 0.8$ L ($P < 0.0001$) with a decrease in PDSAT of 41.1 cm² and in PSSAT of 17.5 cm² at L4-L5. The reduction in PDSAT was significantly larger than that of PSSAT ($P < 0.001$). There was no significant simple relation between changes in SAT subcompartments and their corresponding baseline amount (for PDSAT, $r^2 = 0.12, P = 0.12$, and for PSSAT $r^2 = 0.22, P = 0.057$). There was no significant correlation between changes in PDSAT and PSSAT ($r^2 = 0.145, P = 0.13$). However, the magnitude of change in the subcompartments was significantly related to the change in total body SAT (for PDSAT, $r^2 = 0.50, P = 0.0005$; for PSSAT, $r^2 = 0.31, P = 0.021$).

In the lean group, 11 of 21 women who had repeat studies gained total body SAT as quantified by whole-body MRI. In this 11-member subgroup, the changes in PDSAT and PSSAT did not differ ($P = 0.72$) and were interrelated ($r^2 = 0.45, P = 0.0238$).

DISCUSSION

The results of these and other studies show that the superficial and deep subcompartments of posterior abdominal SAT are distributed differently in the trunk. Fat is deposited to a greater degree in the posterior trunk in obesity, although clinical examination often focuses on the anterior abdomen. We noted that the relative amounts of deep posterior SAT were greater at the level of the L4-L5 intervertebral space than at higher levels in the trunk segment, whereas the superficial SAT portion appeared to be similar in size at the different anatomic levels in lean and obese HIV-infected women.
levels. Thus, PDSAT seems to distribute as an upright truncated cone, with a wider bottom and a narrower top. In contrast, PSSAT is more uniform in the trunk. Although this shape confounds the estimation of SAT, it was sufficiently consistent that the strongest predictor of PDSAT at the L4-L5 in a multiple regression model was SAT at the L2-L3 level.

Variation in the relative amounts of different adipose tissue subcompartments at different levels could affect the relative strengths of relations to metabolic or other variables, despite the fact that measurements of waist circumference (WC) taken at different levels were highly correlated (14). WC is used as an index of abdominal adiposity. Given the fact that there is differential association between abdominal fat depots, i.e., VAT vs. SAT, and metabolic risk and the fact that there is uneven distribution of SAT and VAT, and the consequent site-specific ratio of VAT to SAT, the WCs at different sites might reveal a distinct relation with metabolic risk. In other words, there is a potential of diluting or missing the relation between fat distribution and metabolism with WC from a SAT-dominant lower abdomen, especially among obese subjects. As a further example, there were reports showing that the VAT area from a single slice at L2-L3 correlated better with the total intra-abdominal fat depot (15,16). Therefore, it is conceptually correct to propose to perform the WC measurement at the L2-L3 level.

The larger quantity of PDSAT compared with PSSAT at L4-L5 in the obese group was not apparent in the lean group. Although there was no correlation between the sizes of the 2 subcompartments in obese women, they were correlated with each other in the lean women. These results suggest that different factors may affect the 2 subcompartments, and that they may be biologically distinct.

There was a greater loss of PDSAT than PSSAT in obese HIV+ women after completion of a 12-wk energy-deficit diet and exercise program. Interestingly, the changes in the 2 subcompartments were independent of each other and from their baseline contents. The differential loss of PDSAT in obese HIV+ women suggests that the lipolytic rate may be higher in PDSAT.

Our observation is consistent with previous in vitro studies (10,11). The mechanism underlying the differences is not yet clear. However, it is well recognized among plastic surgeons that superficial and deep abdominal subcutaneous adipose tissue differ (17). Histologically, the superficial layer is supported by guest on October 13, 2017 jn.nutrition.org Downloaded from

### TABLE 2

Coefficient of determination \( (r^2) \) of various independent variables in a stepwise regression analysis and their significance in the prediction of PDSAT at L4-L5 in obese HIV\(^+\) women\(^1\)

<table>
<thead>
<tr>
<th>Dependent</th>
<th>Whole-body SAT</th>
<th>PSSAT at L45</th>
<th>Anterior SAT at L4-5</th>
<th>SAT at ASIS</th>
<th>SAT at greater trochanter</th>
<th>SAT at L2-3</th>
<th>( r^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>L4-5 PDSAT</td>
<td>0.0007</td>
<td>0.0181</td>
<td>0.342</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>0.0007</td>
<td>0.0181</td>
<td>0.342</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
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<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
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<tr>
<td>L4-5 PDSAT</td>
<td>NS</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

\(^1\) Values are the \( P \)-values of each independent variable in a multiple regression model.

\(^2\) The coefficient of determination \( (r^2) \) indicated the association strength between PDSAT and its significant variables in the model.

\(^3\) Void value indicated that the independent variable was not introduced in the model. The significance level was set at \( P < 0.05 \). NS, not significant.

### TABLE 3

Coefficient of determination \( (r^2) \) of various independent variables in a stepwise regression analysis and their significance in the prediction of PDSAT at L4-L5 in lean HIV\(^+\) women\(^1\)

<table>
<thead>
<tr>
<th>Dependent</th>
<th>Whole-body SAT</th>
<th>PSSAT at L45</th>
<th>Anterior SAT at L4-5</th>
<th>SAT at ASIS</th>
<th>SAT at greater trochanter</th>
<th>SAT at L2-3</th>
<th>( r^2 )</th>
</tr>
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<tbody>
<tr>
<td>L4-5 PDSAT</td>
<td>0.0004</td>
<td>NS</td>
<td>0.4622</td>
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<tr>
<td>L4-5 PDSAT</td>
<td>0.0004</td>
<td>NS</td>
<td>0.462</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>0.0004</td>
<td>NS</td>
<td>0.462</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>L4-5 PDSAT</td>
<td>0.0004</td>
<td>NS</td>
<td>0.462</td>
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</tbody>
</table>

\(^1\) Values are the \( P \)-values of each independent variable in a multiple regression model.

\(^2\) The coefficient of determination \( (r^2) \) indicated the association strength between PDSAT and its significant variables in the model.

\(^3\) Void value indicated that the independent variable was not introduced in the model. The significance level was set at \( P < 0.05 \). NS, not significant.
by a dense fibrous network and adipocytes are tightly packed, whereas adipocytes in the deep layer are more loosely arranged. Differences in the blood supply to the superficial and deep layers also were reported (18).

The clinical implications of our observation are related to the association between deep subcutaneous adipose tissue and metabolism and its association strength after controlling for VAT, modified by our ability to make appropriate measurements. It was reported that insulin resistance in obese subjects is associated with deep but not with superficial abdominal SAT (7). A pilot study of large volume lipectomy of SAT, including the posterior abdominal portion, showed improvement in insulin sensitivity (19), whereas a more recent study showed no metabolic changes in response to liposuction of ~10 kg of abdominal fat (20). Nevertheless, these data suggest the overwhelming strength of the association between VAT and insulin sensitivity.

No differential changes in PDSAT or PSSAT were observed in the lean group, and the change in these 2 subcompartment seemed to be related in the subgroup of lean HIV+ women with weight gain.

Although we studied HIV-infected women, the distribution of abdominal SAT did not appear to suggest more HIV-specific manifestation such as lipatrophy or lipodystrophy. The lean women had a low body cell mass as well as body fat, and did not have HIV-associated lipodystrophy (21). The obese patients had a mean total body SAT content of 43 L, which is also not consistent with HIV-associated lipodystrophy. We believe that our findings, derived from comparing 2 HIV groups with differing nutrition status, might well be applicable to other subjects with similar nutritional status.

In conclusion, the distribution of superficial and deep posterior abdominal SAT differs, with more PDSAT in the lower abdomen than PSSAT. Obesity in HIV-infected women was associated with a greater increase in PDSAT than PSSAT. A diet and exercise program in obese, HIV+ women was associated with greater losses of PDSAT than of PSSAT. These in vivo results support previous in vitro observations that the deep subcutaneous adipose tissue subcompartment is more metabolically active than the superficial subcompartment.

LITERATURE CITED