Psoas muscle attenuation measurement with computed tomography indicates intramuscular fat accumulation in patients with the HIV-lipodystrophy syndrome

Martin Torriani,1 Colleen Hadigan,2 Megan E. Jensen,1 and Steven Grinspoon2

1Division of Musculoskeletal Radiology and 2Program in Nutritional Metabolism, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114

Submitted 11 April 2003; accepted in final form 22 May 2003

Torriani, Martin, Colleen Hadigan, Megan E. Jensen, and Steven Grinspoon. Psoas muscle attenuation measurement with computed tomography indicates intramuscular fat accumulation in patients with the HIV-lipodystrophy syndrome. J Appl Physiol 95: 1005–1010, 2003. First published May 23, 2003; 10.1152/japplphysiol.00366.2003.—The human immunodeficiency virus (HIV)-lipodystrophy syndrome is characterized by abnormalities of lipid metabolism, glucose homeostasis, and fat distribution. Overaccumulation of intramuscular lipid may contribute to insulin resistance in this population. We examined 63 men: HIV positive (n = 22), HIV positive without lipodystrophy (n = 20), and age- and body mass index-matched HIV-negative controls (n = 21). Single-slice computed tomography was used to determine psoas muscle attenuation and visceral fat area. Plasma free fatty acids (FFA), lipid profile, and markers of glucose homeostasis were measured. Muscle attenuation was significantly decreased in subjects with lipodystrophy [median (interquartile range), 55.0 (51.0–58.3)] compared with subjects without lipodystrophy [57.0 (55.0–59.0); P = 0.05] and HIV-negative controls [59.5 (57.3–64.8); P < 0.01]. Among HIV-infected subjects, muscle attenuation correlated significantly with FFA (r = –0.38; P = 0.02), visceral fat (r = –0.49; P = 0.002), glucose (r = –0.38; P = 0.02) and insulin (r = –0.60; P = 0.0001) response to a 75-g oral glucose tolerance test. In forward stepwise regression analysis with psoas attenuation as the dependent variable, visceral fat (P = 0.02) and FFA (P < 0.05), but neither body mass index, subcutaneous fat, nor antiretroviral use, were strong independent predictors of muscle attenuation (r² = 0.39 for model). Muscle attenuation (P = 0.02) and visceral fat (P = 0.02), but not BMI, subcutaneous fat, FFA, or antiretroviral use, were strong independent predictors of insulin response (area under the curve) to glucose challenge (r² = 0.47 for model). These data demonstrate that decreased psoas muscle attenuation due to intramuscular fat accumulation may contribute significantly to hyperinsulinemia and insulin resistance in HIV-lipodystrophy patients. Further studies are needed to assess the mechanisms and consequences of intramuscular lipid accumulation in HIV-infected patients.

insulin resistance; protease inhibitor; acquired immunodeficiency syndrome; human immunodeficiency virus

HUMAN IMMUNODEFICIENCY VIRUS (HIV)-infected patients receiving highly active antiretroviral therapy often demonstrate fat redistribution, characterized by subcutaneous fat loss and visceral fat hypertrophy. Changes in fat distribution are often seen in association with insulin resistance and dyslipidemia, and overall lipolysis rates are increased among such patients (17). Excess free fatty acids (FFA) from lipolysis may accumulate in muscle and thereby affect glucose entry and subsequent phosphorylation. Recent studies in this population using proton magnetic resonance (MR) spectroscopy demonstrate increased intramyocellular lipid concentrations (13, 22). Muscle attenuation values obtained with computed tomography (CT) decrease as a function of augmented lipid concentrations and are important independent markers of insulin resistance in non-HIV-infected patients with obesity and Type 2 diabetes (15, 16). However, prior studies using CT scan have not compared muscle attenuation as a surrogate index of intramyocellular fat content in relationship to body composition and metabolic variables in HIV-infected individuals.

MATERIALS AND METHODS

Experimental Subjects and Protocol

Attenuation values of psoas muscles were obtained by CT in 22 HIV-infected men with lipodystrophy syndrome (Lipo), 20 HIV-infected men without lipodystrophy (Nonlipo), and 21 HIV-negative male control subjects (Ctrl) recruited from the multidisciplinary HIV practice at the Massachusetts General Hospital. Subjects were referred for evaluation of observed changes in fat distribution and also were recruited from advertisements seeking HIV-infected patients with and without evidence of fat redistribution.

HIV status was confirmed by enzyme-linked immunosorbent assay and Western blot testing in all subjects. Lipo subjects were selected on the basis of a waist-to-hip ratio of >0.95 and a history of significant change in fat distribution in the trunk, extremities, neck, or face. In all lipodystrophy cases, the presence of changes in fat distribution was con-
firmed by physical examination and scored by a single inves-
tigator as severe (1.5 on a scale of 0–2) in one or more areas. Severe lipodystrophy was scored for changes obvious to the
casual observer and mild-to-moderate lipodystrophy for changes noticeable to the patient and confirmed by the single
investigator. Objective criteria used in the determination of
severe lipodystrophy included, but were not limited to, prom-
inent peripheral venomegaly and a palpable dorsocervical fat
pad. In contrast, HIV-positive, Nonlipo subjects were re-
cruited from advertisements seeking HIV-infected men with-
out changes in fat distribution. Nonlipo subjects were se-
lected on the basis of a waist-to-hip ratio of <0.95 and no
significant fat redistribution in any area on physical exami-
nation. Lipo patients were classified as having significant
peripheral lipoatrophy if they demonstrated moderate or
severe fat loss in the arms or legs. HIV-infected subjects
receiving antiretroviral medications were on a stable regi-
men for >6 wk. One subject in the Lipo group was receiving
stable thyroid hormone replacement. No other subjects were
known to have thyroid disease. To prevent enrollment of
subjects with primary HIV-related wasting, patients with a
body mass index (BMI) >25 kg/m² were excluded from all
groups. Subjects receiving testosterone, growth hormone,
anabolic hormones, glucocorticoid, and antiadiabetic agents,
and megestrol acetate were excluded. Exclusion criteria also in-
cluded known diabetes mellitus, hemoglobin level <9.0 g/dl,
and age >60 and <18 yr.

The non-HIV-infected Ctrl subjects were in good health,
used no medications, and had a waist-to-hip ratio of <0.95.
Written, informed consent was obtained from each subject
before testing, in accordance with the Committee on the use
of Humans as Experimental Subjects of the Massachusetts
Institute of Technology and the Subcommittee on Human
Studies at the Massachusetts General Hospital.

Body composition by CT scan and dual-energy X-ray ab-
sorptiometry (DEXA), and metabolic indexes such as fasting
lipid levels, insulin, glucose, and oral glucose tolerance test
OGTT), plasma FFA, CD4⁺ count, and HIV viral load were
also assessed. Body composition and other endocrine data
have previously been reported in this subpopulation (25, 31).

Experimental Methods

CT attenuation of psoas muscle. All scans were performed
with a LightSpeed CT scanner (General Electric, Milwaukee,
WI). A lateral scout image of the abdomen was obtained to
identify the L₄ pedicle, which served as a landmark for a
single-slice image at this level. Scan parameters for each
image were standardized (144-cm table height, 80 kV, 70 mA,
2 s, 1-cm slice thickness, 48-cm field of view). Bilateral psoas
muscle attenuation values were measured utilizing Impax
workstations (AGFA diagnostic software, version 4; Agfa,
Ridgefield Park, NJ). A circular region of interest with area of
1.5 cm² was placed in the most homogenous area of the
muscle, avoiding visible intra-muscular fat (Fig. 1). A single
measurement was obtained from each side, and average
psoas muscle attenuation value was calculated and ex-
pressed in Hounsfield units (HU).

Body composition analysis. The single cross-sectional CT
image at L₂ was utilized to assess distribution of subcutane-
ous and visceral abdominal fat. Fat attenuation values were
set at –50 to –250 HU as described by Borkan et al. (5), and
intra-abdominal visceral and subcutaneous fat areas were
determined on the basis of tracings obtained utilizing com-
mercial software (Alice, Parexel, Waltham, MA). Abdominal
visceral and subcutaneous fat and the ratio of abdominal
visceral fat to total abdominal cross-sectional area were de-
termined. Fat and fat-free mass were determined by DEXA
with a Hologic 4500 densitometer (Hologic, Waltham, MA).
The technique has a precision error of 3% for fat and 1.5% for
fat-free mass (23). Baseline weight was determined after an
overnight fast, and percent ideal body weight was calculated
on the basis of standard height and weight tables (26).
Waist-to-hip ratio was determined from the circumferential
measurements of the waist at the level of the umbilicus and
the hips at the level of the iliac crest taken with the patient
in an upright standing position.

Hormonal assessment and laboratory methods. Serological
assessment included fasting plasma FFA, triglycerides, and
low-density lipoprotein (LDL), high-density lipoprotein, and
total cholesterol. A standard 75-g OGTT with insulin and
glucose levels, CD4, and HIV viral load were also performed.
All parameters were determined by using previously pub-
lished methods (20, 31).

Statistical analysis. Comparisons were made between the
groups (Lipo vs. Nonlipo, Lipo vs. Ctrl, and Nonlipo vs. Ctrl)
by the Wilcoxon rank-sum test. χ² analysis was used to
assess group differences for categorical variables. Univariate
regression analyses were performed, comparing CT attenua-
tion values and indexes of body fat and composition among
all HIV-infected patients. Forward stepwise regression anal-
yses, P = 0.1 to enter the model, was performed to determine
relevant factors contributing to muscle attenuation and hy-
perinsulinemia. Statistical significance was defined as P <
0.05. Results are median plus interquartile range. Statistical
analyses were made by using JMP Statistical Database Soft-
ware (SAS Institute, Cary, NC).

RESULTS

Age and BMI were not significantly different be-
tween the groups (Table 1). As previously reported, no
significant difference in whole body fat mass measured
by DEXA was detected between groups (31). Regional
trunk fat was increased, and extremity fat decreased in
Lipo compared with Nonlipo and Ctrl subjects. The
Nonlipo and Ctrl groups showed no significant differ-
ence in either truncal or extremity fat. Lipo subjects
demonstrated significantly increased visceral fat area
and visceral fat to total abdominal cross-sectional area
determined by CT, compared with Nonlipo and Ctrl

J Appl Physiol • VOL 95 • SEPTEMBER 2003 • www.jap.org
Table 1. Group comparison by lipodystrophy and HIV status

<table>
<thead>
<tr>
<th>HIV-Infected Lipodystrophic Patients (n = 22)</th>
<th>HIV-Infected Nonlipodystrophic Patients (n = 20)</th>
<th>Normal Controls (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>47 (38–50)</td>
<td>41 (37–44)</td>
</tr>
<tr>
<td>Waist-to-tiep ratio</td>
<td>0.99 (0.97–1.04)</td>
<td>0.91 (0.88–0.93)</td>
</tr>
<tr>
<td>CD4+ T cells, no./mm³</td>
<td>371 (144–565)</td>
<td>313 (153–434)</td>
</tr>
<tr>
<td>HIV viral load, copies/ml</td>
<td>89 (50–13,150)</td>
<td>10,475 (73–42,925)</td>
</tr>
<tr>
<td>Duration of HIV, yr</td>
<td>9 (6–10)</td>
<td>6 (4–8)</td>
</tr>
<tr>
<td>NRTI use, %</td>
<td>100%</td>
<td>60</td>
</tr>
<tr>
<td>PI use, %</td>
<td>90%</td>
<td>45</td>
</tr>
</tbody>
</table>

Body composition

| BMI, kg/m²                                    | 24.6 (22.2–26.6)                               | 24.4 (23.3–25.9)          | 24.8 (22.7–26.1)         |
| Whole body fat by DEXA, kg                   | 14.1 (12.0–18.4)                               | 14.6 (11.0–18.9)          | 16.7 (13.4–19.4)         |
| Trunk fat/total fat by DEXA, kg              | 0.61 (0.56–0.65)                               | 0.46 (0.41–0.49)          | 0.49 (0.42–0.52)         |
| Extremity fat/total fat by DEXA, kg          | 0.31 (0.27–0.35)                               | 0.46 (0.44–0.51)          | 0.44 (0.42–0.51)         |
| Visceral fat area by CT, cm²                 | 158 (114–196)                                  | 76 (51–112)               | 88 (62–116)              |
| Subcutaneous fat area by CT, cm²             | 118 (60–184)                                   | 118 (99–181)              | 159 (124–225)            |
| VAT/abdominal cross-sectional area by CT     | 0.25 (0.18–0.31)                               | 0.15 (0.11–0.18)          | 0.14 (0.12–0.20)         |
| Psoas muscle density by CT, HU               | 55.0 (51.0–58.3)                               | 57.0 (55.0–59.0)          | 59.5 (57.3–64.8)         |

Metabolic status

| FFA, mmol/l                                  | 0.62 (0.39–0.73)                               | 0.56 (0.52–0.76)          | 0.58 (0.49–0.78)         |
| HDL cholesterol, mg/dl                      | 36 (30–41)                                    | 44 (36–50)                | 47 (40–56)               |
| LDL cholesterol, mg/dl                      | 114 (82–143)                                  | 92 (76–123)               | 96 (77–122)              |
| Triglycerides, mg/dl                        | 189 (124–378)                                 | 174 (118–192)             | 75 (50–101)              |
| Total cholesterol, mg/dl                    | 193 (160–223)                                 | 164 (141–198)             | 169 (139–193)            |
| Fasting glucose, mg/dl                      | 93 (85–98)                                    | 94 (89–97)                | 90 (85–95)               |
| OGTT glucose response, AUC [mg/dl (120 min)]| 18,330 (15,435–19,883)                        | 16,493 (14,760–18,518)    | 14,475 (13,155–16,475)   |
| Fasting insulin, μU/ml                      | 11.5 (8.4–21.3)                               | 8.7 (7.4–12.8)            | 7.8 (6.6–8.5)            |
| OGTT insulin response, AUC [μU/ml (120 min)]| 8,589 (3,794–20,539)                          | 4,781 (3,856–6,398)       | 4,478 (3,508–6,190)      |

Values are medians with interquartile range; n, no. of subjects; HIV, human immunodeficiency virus; BMI, body mass index; DEXA, dual-energy X-ray absorptiometry; CT, computed tomography; VAT, abdominal visceral fat; HDL, high-density lipoproteins; LDL, low-density lipoproteins; AUC, area under the curve; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; FFA, free fatty acids; OGTT, oral glucose tolerance test; NA, not applicable; HU, Hounsfield units. *P < 0.01 and †P < 0.05. For HIV-infected lipodystrophic vs. HIV-infected nonlipodystrophic patients, ‡P < 0.01 and §P < 0.05. For HIV-infected nonlipodystrophic patients vs. controls, *P < 0.05.

Subjects. No significant differences in visceral fat area were observed between Nonlip and Ctrl subjects. CD4 cell count and HIV viral load were not significantly different between HIV-infected groups, although duration of HIV, protease inhibitor (PI) use, and nucleoside reverse transcriptase inhibitor (NRTI) use were greater in lipodystrophic patients compared with the Nonlip group (Table 1).

The mean psoas muscle attenuation value measured by CT was significantly lower in the Lipo subjects, compared with Nonlip and Ctrl subjects (Fig. 2). A significant difference was also seen between attenuation values of Nonlip and Ctrl (P < 0.05). Among HIV-infected subjects, BMI, waist-to-tiep ratio, and body composition measurements were highly inversely related to psoas muscle attenuation (Table 2). Trunk fat measured by DEXA (r = −0.50, P = 0.002), visceral fat by CT (r = −0.49, P = 0.002), and whole body fat by DEXA (r = −0.32, P = 0.05) correlated inversely with psoas muscle attenuation. In contrast, subcutaneous fat by CT was not significantly associated with psoas attenuation values. Additionally, plasma FFA, LDL, total cholesterol, and glucose and insulin area under the curve (AUC) during OGTT were significantly inversely related to muscle attenuation determined by CT scan (Table 2).

A forward stepwise regression analysis was performed with psoas muscle attenuation value as the dependent variable (Table 3). Visceral fat, BMI, plasma FFA, subcutaneous fat area, and PI and NRTI use were tested as independent variables utilizing a probability to enter of 0.1. The resulting whole model r² value was 0.39, and it demonstrated that visceral fat (P = 0.02) and plasma FFA (P < 0.05), but not BMI, were significant predictors for psoas muscle attenuation.
Table 2. Univariate correlations of body composition, WHR, and metabolic status with psoas muscle density in HIV-infected subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Psoas Muscle Density, HU</th>
<th>r value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>-0.43</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>WHR</td>
<td>-0.54</td>
<td>0.0006</td>
<td></td>
</tr>
<tr>
<td>Visceral fat by CT</td>
<td>-0.49</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous fat by CT</td>
<td>-0.23</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Whole body fat by DEXA</td>
<td>-0.32</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Trunk fat by DEXA</td>
<td>-0.50</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Metabolic status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFA</td>
<td>-0.38</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>-0.42</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-0.30</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>-0.47</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Glucose response to OGTT (AUC)</td>
<td>-0.38</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>-0.32</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Insulin response to OGTT (AUC)</td>
<td>-0.60</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; WHR, waist-to-hip ratio

subcutaneous fat or antiretroviral use, were strong predictors of psoas muscle attenuation. To determine the effect of muscle attenuation on hyperinsulinemia we also performed forward stepwise regression analysis for insulin AUC (Table 3). Psoas attenuation, visceral fat, BMI, subcutaneous fat area, FFA, and PI and NRTI use were tested as independent variables utilizing a probability to enter of 0.1. Both muscle attenuation (P = 0.02) and visceral fat (P = 0.02), but not BMI, subcutaneous fat, FFA, or antiretroviral use, were strong independent predictors of insulin AUC (r² = 0.47 for model). This model indicated that a decrease of 1 HU in psoas attenuation (2% of median, 56 HU) predicted an increase in insulin AUC of 776 μIU/ml (14% of median, 5,491 μIU/ml).

**DISCUSSION**

The HIV-lipodystrophy syndrome is characterized by increased visceral adiposity, loss of subcutaneous extremity fat, insulin resistance, and dyslipidemia (9, 10, 27, 36). The mechanisms of the syndrome are unknown and may be related to PI or NRTI inhibitor effects (8, 21) or an interaction of drug and nondrug factors. In addition, it is not known whether the HIV-lipodystrophy syndrome represents a single pathophysiological entity or several distinct subsyndromes. Hypertriglyceridemia is associated with increased concentrations of muscle lipid and insulin resistance in animal models (11), healthy subjects (3), and obese and Type 2 diabetic subjects (15, 29). Intramuscular lipid may contribute to skeletal muscle insulin resistance through inhibition of insulin signaling at phosphatidylinositol 3-kinase kinase and related inhibition of glucose transport (30). The extent and metabolic consequences of intramuscular lipid accumulation in HIV-infected patients with fat redistribution remains unknown.

In non-HIV-infected patients, data obtained with CT have been demonstrated in patients with HIV infection and fat redistribution receiving highly active antiretroviral therapy (17, 24, 32, 33, 36). Increased lipolysis was recently shown to be a strong predictor of insulin resistance in HIV-infected men (17), and improved insulin sensitivity was demonstrated after acute inhibition of lipolysis with acipimox in this population (18). Results from the present study extend these prior observations and demonstrate increased intramuscular lipid in HIV-infected patients, in association with fat distribution and FFA. Furthermore, our data are in agreement with the results of Behrens et al. (1) demonstrating hyperinsulinemia and reduced insulin-mediated glucose uptake of skeletal muscle in HIV-lipodystrophic patients with increased levels of FFA.

Table 3. Forward stepwise regression analysis of HIV-infected patients

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Parameter Estimate</th>
<th>Stepwise P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoas muscle attenuation (r² = 0.39 for whole model, P = 0.1 to enter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visceral fat by CT, cm²</td>
<td>-0.024</td>
<td>0.02</td>
</tr>
<tr>
<td>Plasma FFA, mmol/l</td>
<td>-6.14</td>
<td>0.049</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>-0.37</td>
<td>0.10</td>
</tr>
<tr>
<td>Subcutaneous fat by CT, cm²</td>
<td>NA</td>
<td>0.89</td>
</tr>
<tr>
<td>PI use</td>
<td>NA</td>
<td>0.49</td>
</tr>
<tr>
<td>NRTI use</td>
<td>NA</td>
<td>0.82</td>
</tr>
<tr>
<td>Insulin AUC (r² = 0.47 for whole model, P = 0.1 to enter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visceral fat by CT, cm²</td>
<td>53.05</td>
<td>0.02</td>
</tr>
<tr>
<td>Psoas muscle attenuation, HU</td>
<td>-776.25</td>
<td>0.02</td>
</tr>
<tr>
<td>Plasma FFA, mmol/l</td>
<td>NA</td>
<td>0.31</td>
</tr>
<tr>
<td>Subcutaneous fat by CT, cm²</td>
<td>NA</td>
<td>0.38</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>NA</td>
<td>0.21</td>
</tr>
<tr>
<td>PI use</td>
<td>NA</td>
<td>0.53</td>
</tr>
<tr>
<td>NRTI use</td>
<td>NA</td>
<td>0.67</td>
</tr>
</tbody>
</table>
Visceral fat area, but not subcutaneous fat area, was highly related to CT attenuation. In stepwise regression modeling, visceral fat remained strongly associated with muscle attenuation in a model including PI and NRTI use as well as BMI. These data are consistent with and extend those of Gan et al. (13), demonstrating a relationship between visceral, but not subcutaneous, fat and intramyocellular lipid by proton MR spectroscopy in this population. Our results support the hypothesis that the lipodystrophy syndrome represents several distinct subsyndromes in which lipoatrophy per se is not associated with intramuscular lipid accumulation and is related to use and duration of NRTI therapy (2, 12). In contrast, our data suggest that visceral adiposity and a marked metabolic syndrome is associated with intramuscular lipid accumulation. Although the mechanism of visceral hypertrophy is not known, preliminary data suggest that use of PIs may contribute to visceral fat accumulation and to related insulin resistance and dyslipidemia (10). Of note, the Nonlipo group also demonstrated decreased psoas muscle attenuation, although not to the same degree as the Lipo patients. This suggests a spectrum of metabolic derangement among HIV-infected patients that is not entirely defined by the presence of fat redistribution.

We demonstrate that muscle attenuation is a strong predictor of hyperinsulinemia, suggesting significant metabolic consequences of intramuscular lipid accumulation in this population. Our data suggest an overall schema whereby visceral fat hypertrophy may contribute to intramuscular fat accumulation and hyperinsulinemia. Increased lipolysis in association with visceral adiposity may result in increased FFA levels that accumulate in the muscle, particularly if there is relatively less subcutaneous or extremity fat to serve as a depot for fat substrate. In turn, excess intramyocellular lipid may reduce glucose uptake into the muscle through effects on phosphatidylinositol 3-kinase and thereby contribute to insulin resistance.

Because of the cross-sectional nature of this study, we cannot determine causality, and it is also plausible that insulin resistance as a primary event impairs insulin-mediated inhibition of lipolysis, resulting in excess FFA and lipid accumulation in the muscle. Furthermore, Luzi et al. (22) demonstrated decreased lipid oxidation rates in association with increased intramyocellular lipid accumulation among HIV-infected patients receiving antiretroviral therapy, but regional and whole body lipolytic rates were not quantified.

Although skeletal muscle fat content can be estimated on the basis of X-ray attenuation value by CT (6, 7, 14, 28), this methodology is incapable of directly measuring muscle lipid content, and distinction of intramyocellular and extramyocellular fat is not possible. Proton MR spectroscopy has been recently validated as a specific and sensitive method to directly quantify skeletal muscle lipids (4, 35), with reliable results correlating intramyocellular lipids with biopsy samples (19) and insulin sensitivity (34). This technique has been successfully employed by Gan et al. (13), who found increased intramuscular lipid in association with insulin resistance in HIV-lipodystrophy patients. Nevertheless, single-slice CT scanning, as performed in this study, appears to be effective for assessment of body composition and overall psoas muscle adiposity overcoming anatomic limitations of MR spectroscopy that is limited to two muscles of the lower leg. The capability of quantifying attenuation in a variety of muscles as well as fat distribution around muscle represent a significant advantage of CT methodology. The widespread availability of CT, relative low cost, and prompt acquisition of data also make it well suited for large-scale clinical investigation.

In summary, this study demonstrates decreased psoas muscle attenuation in HIV-infected patients with evidence of the lipodystrophy syndrome. Diminished psoas attenuation is associated with abnormal body composition and lipid and glucose metabolism in this population. Our data support the hypothesis that overaccumulation of intramuscular lipids contributes to decreased insulin sensitivity and hyperinsulinemia in this population. Further studies investigating the pathogenesis of intramuscular lipid accumulation and effects on glucose homeostasis are necessary to determine optimal treatment strategies for dyslipidemia and insulin resistance in HIV-infected patients.

We thank the nursing and bionutrition staff of the General Clinical Research Center at the Massachusetts General Hospital for their dedicated patient care.

DISCLOSURES

This study was funded in part by National Institutes of Health Grants DK-59535, RR-300088, and RR-01066.

REFERENCES

8. Carr A, Miller J, Law M, and Cooper DA. A syndrome of lipaopaathy, lactic acidemia and liver dysfunction associated


