Alterations in liver, muscle, and adipose tissue insulin sensitivity in men with HIV infection and dyslipidemia


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Dyslipidemia is common in patients with HIV infection. In this study, a two-stage euglycemic hyperinsulinemic clamp, with infusion of stable isotope-labeled tracers, was used to evaluate insulin action in skeletal muscle, liver, and adipose tissue in HIV-infected men with dyslipidemia (HIV-DL); plasma triglyceride >250 mg/dl and HDL <45 mg/dl; n = 12), HIV-infected men without dyslipidemia (HIV w/o DL; n = 12), and healthy men (n = 6). Basal rates of glucose production (glucose Ra), glucose disposal (glucose Rd), and lipolysis (palmitate Ra) were similar between groups. The relative suppression of glucose Ra (63% ± 4%, P = 0.02) and inversely with plasma IL-6 (4% ± 3%, P = 0.001). We conclude that dyslipidemia in HIV-infected men is indicative of multiorgan insulin resistance, and circulating adipokines may be important in the pathogenesis of impaired insulin action.

METHODS

Subjects. A total of 30 men participated in this study: 12 with HIV-DL [43 ± 3 yrs old; 7 receiving protease inhibitor (PI)-based HAART; 5 receiving non-PI-based HAART]; 12 with HIV w/o DL [41 ± 3 yr old; 6 naive to therapy and 6 receiving HAART, of whom 2 were receiving PI-based HAART]; and six healthy male volunteers without known illnesses (35 ± 5 yr old). Subjects in each group were matched on BMI and percent body fat. Subjects were considered to have dyslipidemia if they had a serum triglyceride concentration ≥250 mg/dl and a serum HDL-cholesterol concentration ≤45 mg/dl. All subjects had been on their current antiretroviral regimens for >6 mo before enrollment. All subjects were sedentary (<2 h/wk of exercise), consumed fewer than three alcoholic beverages per week, did not have hepatitis C or B infection, had not engaged in recreational drug use in the 6 mo before the study, and were weight stable (<2% weight change in the 3 mo before the study). All subjects had normal plasma testosterone concentration. Subjects with diabetes, significant organ system dysfunction, altered thyroid function, or uncontrolled hypertension were excluded. In addition, subjects who were taking medications known to affect glucose or lipid metabolism, such as β-blockers, β-agonists, and corticosteroids, were excluded from participation. This study was approved by the Human Studies Committee.
and the General Clinical Research Center (GCRC) Scientific Advisory Committee of Washington University School of Medicine. Written informed consent was obtained from all subjects before their participation.

**Body composition assessment.** Total body fat and fat-free (FFM) mass were determined using dual-energy X-ray absorptiometry (Hologic QDR 2000, Waltham, MA), as described previously (29). Abdominal (subcutaneous and intra-abdominal) fat mass was quantified using proton magnetic resonance imaging (Siemens, Iselin, NJ). Eight serial cross-sectional images obtained at the level of the L2-L3 interspace were analyzed for abdominal subcutaneous and intra-abdominal adipose tissue content (Analyze Direct). Intrahepatic lipid content was quantified using proton magnetic resonance spectroscopy (MRS; 1.5T whole body system; Magnetom, Sonata; Siemens, Erlangen, Germany) (71). Intrahepatic lipid content (% water signal) was determined using proton magnetic resonance spectroscopy (MRS; 1.5T whole body system; Magnetom, Sonata; Siemens, Erlangen, Germany) (71). Intrahepatic lipid content (% water signal) was determined using proton magnetic resonance spectroscopy (MRS; 1.5T whole body system; Magnetom, Sonata; Siemens, Erlangen, Germany) (71).

**Isotope infusion protocol.** Subjects were admitted to the in-patient unit of the GCRC at Washington University School of Medicine in the evening before the isotope infusion study. All study participants consumed a diet providing ≥25 kcal/kg body wt and containing ≥60% of calories from carbohydrate for 3 days before admission. Dietary compliance was assessed by reviewing 3-day food recall records obtained from each subject before admission to the GCRC. At 1900 on the day of admission, subjects consumed a standardized meal, containing a total of 12 kcal/kg body wt (55% of total energy from carbohydrates, 30% from fat, and 15% from protein). At 2000, subjects consumed a liquid formula (Ensure; Ross Laboratories, Columbus, OH), containing 250 kcal (40 g carbohydrates, 6.1 g fat, and 8.8 g protein) and then fasted until the completion of the study the following day.

The following morning at 0530, a catheter was inserted into an antecubital vein to administer stable isotope-labeled tracers, and a second catheter was inserted into a hand vein on the opposite arm; the hand was heated to 55°C using a thermostatically controlled box to obtain arterialized venous blood samples (24). At 0700, a primed (22.5 μmol/kg), constant (0.25 μmol·kg⁻¹·min⁻¹) intravenous infusion of [6,6-2H₂]glucose was started. At 0900, a constant (0.04 μmol·kg⁻¹·min⁻¹) infusion of potassium [2,2-2H₂]palmitate dissolved in 25% human albumin (Centeon, Kankakee, IL) was started. All tracers were obtained from Cambridge Isotope Laboratories (Andover, MA). After a baseline period (0–210 min), a two-stage hyperinsulinemic euglycemic clamp was started (Fig. 1). During stage 1 of the clamp, a primed (80 μU·m⁻²·min⁻¹ × 5 min, 40 μU·m⁻²·min⁻¹ × 5 min) constant (20 μU·m⁻²·min⁻¹) infusion of regular human insulin was started and continued for 4 h. The infusion rates for [3H]palmitate and [3H]glucose were reduced by 50% of the basal infusion rate during stage 1 and by 75% of the basal infusion rate during stage 2 to allow for the anticipated decline in glucose and palmitate Rₜ during insulin infusion. A plasma glucose concentration of 5.5 mM (100 mg/dl) was maintained by a variable rate infusion of 20% dextrose containing 2.5% [6,6-2H₂]glucose.

Blood samples were obtained before the isotope infusion was begun to determine background isotope enrichments and every 10 min during the last 30 min of the basal period and during each stage of the clamp procedure to determine plasma substrate and hormone concentrations and substrate kinetics. Blood samples were also obtained every 10 min throughout the clamp to determine plasma glucose concentrations and were used to adjust the variable dextrose infusion rate.

An automated metabolic measurement cart with a ventilated hood system (SensorMedics, Yorba Linda, CA) was used to quantify O₂ consumption and CO₂ production rates. Respiratory gas exchange measurements were made during the last 20 min of the basal, stage 1, and stage 2 periods of the euglycemic hyperinsulinemic clamp procedure; data obtained during the final 15 min were used to calculate energy expenditure and substrate utilization rates. Urine was collected for 24 h, beginning in the evening before the euglycemic hyperinsulinemic clamp procedure, to determine urinary nitrogen excretion.

**Sample analyses.** Plasma glucose concentration was determined using an automated glucose analyzer (Yellow Springs Instruments, Yellow Springs, OH). Hemoglobin A₁C was determined from whole blood by use of an automated cation exchange HPLC method (Bio-Rad Variant Hb A₁C Program; Bio-Rad Laboratories, Diagnostic Group, Hercules, CA) (20). Plasma insulin (19), C-peptide, and leptin (33) concentrations were measured by radioimmunoassay. Plasma total cholesterol, HDL-cholesterol, and triglycerides were determined enzymatically using commercially available kits (Roche/Hitachi 747 Analyzer; Roche Diagnostics, Indianapolis, IN); LDL-cholesterol was calculated using the Friedewald equation (14). Commercial enzyme-linked immunosorbent assays kits were used to measure plasma adiponectin (B-bridge International, Sunnyvale, CA), plasma IL-6, and TNF-α (Quaintkine High Sensitive; R & D Systems, Minneapolis MN).

The tracer-to-trace ratio (TTR) of palmitate and glucose in plasma was quantified using gas chromatography-mass spectrometry. Acetone was used to precipitate plasma proteins, and hexane was used to extract plasma lipids. The aqueous phase was dried by Speed-Vac centrifugation (Savant Instruments, Farmingdale, NY). Heptfluorobutyric anhydride was used to form a heptfluorobutyric derivative of glucose. Free fatty acids (FFA) were isolated from plasma and converted to their methyl esters. Ions were selectively monitored to determine TTR, as described previously (29–31). Instrument response was calibrated by using standards of known isotopic enrichment.

Urinary total nitrogen excretion was measured using modified Kjeldahl analysis, as described previously (20, 40), and used to calculate the nonprotein respiratory quotient. Carbohydrate oxidation rate was calculated on the basis of the gas exchange ratio, as described previously (13).

**Calculations.** Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as [plasma glucose concentration (mM) × plasma insulin concentration (μU/ml)/22.5] (28).

Plasma palmitate and glucose Rₜ were calculated by dividing each tracer infusion rate by the average arterial TTR obtained during the last 30 min of each stage of the clamp (41, 49), as the plasma palmitate and glucose enrichments were constant during the sampling periods. Glucose Rₜ was calculated as the sum of endogenous glucose Rₜ plus infused glucose. Nonoxidative glucose disposal was determined by subtracting carbohydrate oxidation rate from the rate of whole body glucose Rₜ.

![Fig. 1. Schematic representation of isotope infusion protocol. Stage 1, low-dose insulin infusion (plasma insulin concentration ~30 μU/ml); stage 2, high-dose insulin infusion (plasma insulin concentration ~75 μU/ml).](image-url)
Statistical analyses. One-way analysis of variance (ANOVA) was used to compare group body composition, hormone and substrate concentrations, and glucose and lipid kinetics, followed by Tukey’s post hoc testing where indicated. Pearson correlation was used to assess associations between continuous variables. One-way ANOVA by ranks was performed for nonnormally distributed data. Comparison of current antiretroviral medication use by group was performed using χ² analysis with Fisher’s exact test. Significance was accepted at α = 0.05. Group virologic characteristics are reported as median with 25 and 75% confidence intervals. All other values are reported as means ± SE.

RESULTS

Clinical characteristics. The duration of HIV infection, based on the date of the subject’s first known positive HIV antibody test, was similar in HIV-DL (5.5 ± 1.1 yr) and HIV w/o DL groups (5.6 ± 0.7 yr). Serum CD4 cell concentration was not different between HIV-DL (616 ± 71 cells/mm³) and HIV w/o DL groups (496 ± 46 cells/mm³). Viral load was higher in the HIV w/o DL (10,172 ± 5,512 log copies/ml) than in the HIV-DL group (185 log copies/ml in one subject only; all others had <40 copies/ml), because the HIV w/o DL group included subjects who were not receiving HAART. A greater proportion of subjects with HIV-DL (all subjects) than with HIV w/o DL (6 of 12 subjects, P = 0.01) were receiving antiretroviral medications. The HIV-infected groups were not different with respect to current stavudine (5 of 12 subjects with HIV-DL, 1 of 12 subjects with HIV w/o DL) or lamivudine use (8 of 12 subjects with HIV-DL, 4 of 12 subjects with HIV w/o DL). However, there was a tendency toward a greater use of PI among patients with HIV-DL (7 of 12 subjects: 2 receiving nelfinavir, 4 receiving indinavir, and 1 receiving atazanavir) than HIV w/o DL (2 of 12 subjects: 1 receiving lopinavir/ritonavir, 1 receiving nelfinavir, P = 0.1).

Body composition. FFM and percent body weight as fat were not different between groups (Table 1). However, the ratio of visceral adipose tissue to total abdominal adipose tissue and intrahepatic lipid content was much greater in subjects with HIV-DL than in subjects with HIV w/o DL and control subjects. Among patients with HIV infection, intrahepatic fat content correlated directly with palmitate Rₚ during stage 1 of the clamp (r = 0.57, P = 0.02).

Substrate and hormone concentrations. By design, subjects with HIV-DL had higher serum triglyceride and lower HDL-cholesterol concentrations than the other groups. Although fasting blood glucose concentrations were within the normal range and no subjects had diabetes, the HIV-DL group had a higher mean fasting blood glucose concentration than the other groups. Mean fasting blood glucose concentration did not differ in subjects with HIV infection treated with PI (5.39 ± 0.11 mM) compared with those not receiving PI (5.38 ± 0.11 mM) within the HIV-DL group. Fasting plasma insulin concentration and insulin-to-C-peptide ratio were greater in subjects with HIV-DL than in the other groups (Table 2).

Table 2. Fasting plasma substrate and hormone concentration

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>HIV w/o DL</th>
<th>HIV-DL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride, mg/dl</td>
<td>135±21</td>
<td>119±18</td>
<td>445±48*</td>
</tr>
<tr>
<td>HDL-cholesterol, mg/dl</td>
<td>46±3</td>
<td>46±2</td>
<td>34±1†</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>166±15</td>
<td>180±11</td>
<td>235±13*</td>
</tr>
<tr>
<td>LDL-cholesterol, mg/dl</td>
<td>93±10</td>
<td>109±10</td>
<td>118±13</td>
</tr>
<tr>
<td>Glucose, mM</td>
<td>4.9±0.1</td>
<td>5.1±0.1</td>
<td>5.4±0.1*</td>
</tr>
<tr>
<td>FFA, mM</td>
<td>380±50</td>
<td>310±40</td>
<td>420±40</td>
</tr>
<tr>
<td>Insulin, µU/ml</td>
<td>6±1</td>
<td>62±1</td>
<td>12±2*</td>
</tr>
</tbody>
</table>

Values are means ± SE. HDL, high-density lipoprotein; LDL, low-density lipoprotein; FFA, free fatty acid. *Significantly different from control and HIV w/o DL values, P < 0.05; †significantly different from HIV w/o DL, P = 0.01; P = 0.1 vs. control.

During the hyperinsulinemic euglycemic clamp procedure, insulin infusion caused a similar increase in plasma insulin concentrations to 37 ± 3, 32 ± 2, and 37 ± 2 µU/ml during stage 1, and to 89 ± 8, 80 ± 3, and 79 ± 4 µU/ml during stage 2 in healthy volunteer, HIV w/o DL, and HIV-DL groups, respectively (P = nonsignificant between groups at each stage).

Basal glucose Rₐ was not different between control (11.5 ± 0.7 µmol·kg⁻¹·min⁻¹), HIV w/o DL (12.0 ± 0.6 µmol·kg⁻¹·min⁻¹), and HIV-DL (12.3 ± 0.5 µmol·kg⁻¹·min⁻¹). Glucose Rₚ declined during stage 1 (Fig. 2B) in all groups and was fully suppressed (~0) during stage 2 (data not shown). The ability of low-dose insulin infusion to suppress glucose Rₚ during stage 1 of the clamp was blunted in subjects with HIV-DL compared with HIV w/o DL and healthy volunteer groups (Figs. 2B and 3). Glucose Rₚ increased in a stepwise manner in all groups during each stage of the hyperinsulinemic euglycemic clamp procedure (Fig. 3C). However, the relative increase in glucose Rₚ above baseline during stage...
2 of the clamp procedure was almost twofold lower in subjects with HIV-DL than in subjects with HIV w/o DL and healthy volunteers (P < 0.001; Fig. 3C).

Basal palmitate Ra was not different between control (1.03 ± 0.08 μmol·kg FFM⁻¹·min⁻¹), HIV w/o DL (0.81 ± 0.08 μmol·kg FFM⁻¹·min⁻¹), and HIV-DL (1.09 ± 0.10 μmol·kg FFM⁻¹·min⁻¹). However, the ability of low-dose insulin infusion to suppress palmitate Ra during stage 1 of the clamp was blunted in subjects with HIV-DL compared with subjects with HIV w/o DL and healthy volunteers (Figs. 2A and 3). In addition, plasma FFA concentration during low-dose insulin infusion was twofold greater in HIV-DL (185 ± 29 mM) than in HIV w/o DL (87 ± 10 mM) and control (82 ± 5 mM, P < 0.03).

Energy expenditure and substrate oxidation. Resting energy expenditure was greater in HIV-DL (30.9 ± 0.7 kcal/kg FFM) than in control (28.2 ± 0.4 kcal/kg FFM, P = 0.04) but was not different in subjects with HIV w/o DL (29.8 ± 0.8 kcal/kg FFM). Insulin infusion stimulated oxidative and nonoxidative glucose utilization in all groups. The increase in nonoxidative glucose disposal was blunted in subjects with HIV-DL compared with the other groups (Figs. 3D, P = 0.004). However, nonoxidative glucose disposal as a proportion of total glucose disposal was not significantly different between HIV-DL (70 ± 2%), HIV w/o DL (75 ± 2%), and healthy volunteer groups (77 ± 2%) during stage 2 of the clamp. Fat oxidation rates were similar between groups during basal conditions and declined in a stepwise manner during each stage of the hyperinsulinemic euglycemic clamp procedure (data not shown).

Relationships between adipokines and insulin action. Basal plasma adiponectin concentrations were inversely correlated with the percent suppression of basal glucose production (glucose Ra) during low-dose insulin infusion (r = 0.44, P = 0.02), and stimulation of glucose disposal (glucose Rd) during high-dose insulin infusion (r = 0.48, P < 0.01). Basal plasma adiponectin concentrations were not related to percent suppress-
tion of lipolysis (palmitate $R_{p}$) during low-dose insulin infu-
sion. Basal plasma IL-6 concentrations correlated with the percent suppression of basal glucose $R_{b}$ ($r = -0.49$, $P = 0.006$) during low-dose insulin infusion and the percent in-
crease of glucose disposal during high-dose insulin infusion ($r = -0.43$, $P = 0.02$).

**DISCUSSION**

Dyslipidemia is common in HIV-infected people, particu-
larly those receiving HAART. The results of the present study
demonstrate that dyslipidemia in patients with HIV infection is
a marker of insulin resistance in liver, skeletal muscle, and
adipose tissue. Moreover, decreased plasma adiponectin and
increased plasma IL-6 concentrations were associated with
impaired insulin-mediated suppression of endogenous glucose
production and stimulation of glucose disposal, suggesting that
alterations in adipocyte production might contribute to insulin
resistance.

Hypertriglyceridemia in patients with HIV infection is
caused by both an increase in hepatic VLDL-triglyceride se-
cretion into the systemic circulation (35, 38) and impaired
clearance of plasma VLDL-triglyceride and chylomicrons (5,
37). Our data suggest that both alterations in body fat distri-
bution and adipose tissue insulin resistance might be re-
sponsible for stimulating VLDL-triglyceride production by increas-
ing hepatic fatty acid availability (24). Although body fat mass
was not different between groups, subjects with HIV-DL had a
greater amount of intrahepatic and intraperitoneal (visceral) fat
than those without dyslipidemia. Therefore, these sites can
provide additional substrate for VLDL-triglyceride production
by releasing fatty acids within hepatocytes and into the portal
vein for direct delivery to the liver. In addition, we found the
ability of insulin to suppress lipolysis of adipose tissue triglyc-
eride was impaired in subjects with HIV-DL, which would also
increase fatty acid release into the systemic circulation and
delivery to the liver. Antiretroviral therapy itself has been
shown to decrease cellular CD36 content (39), which could
blunt the clearance of circulating VLDL-triglyceride (17).

High plasma triglyceride concentrations are often associated
with low plasma HDL concentrations (10). An increase in
circulating VLDL increases the transfer of triglycerides from
VLDL to HDL, which leads to increased HDL clearance and
decreased plasma HDL concentration (22). Therefore, it is
likely that the increase in plasma triglycerides in our subjects
with HIV-DL contributed to their low plasma HDL-cholesterol
concentrations. The combination of increased plasma triglyc-
erides and decreased HDL-cholesterol increases the risk of
CHD (11, 18) and may be an important reason for the increase
in myocardial infarctions and death from CHD observed in
patients with HIV infection (1, 15).

Insulin resistance in patients with HIV-DL is not always
apparent from the results of standard clinical studies, such as
fasting blood glucose concentration or an oral glucose toler-
ance test; our subjects with HIV-DL had normal fasting blood
glucose concentrations. In addition, studies from other groups
have also found that most subjects with HIV-DL do not have
fasting hyperglycemia or hyperinsulinemia (42). Our results
suggest that provocative testing may be necessary to unmask
insulin resistance. Although subjects with HIV-DL had normal
basal glucose production, glucose disposal, and lipolytic rates,
we found evidence of multiorgan insulin resistance by using
the hyperinsulinemic euglycemic clamp procedure. These re-
sults suggest that most subjects with HIV-DL have impaired
insulin action and, therefore, are at increased risk of developing
diseases that are linked with insulin resistance, such as diabe-
tes and CHD (32, 36).

The HIV-lipodystrophy syndrome can be difficult to diag-
nose because there is no uniformly accepted, objective clinical
criteria. Patients who have this syndrome, diagnosed by com-
monly used clinical criteria (43) or by using the Carr lipody-
strophy score (7), often have dyslipidemia. In fact, 8 of 12
subjects with HIV-DL met the clinical criteria of HIV-lipody-
strophy and 11 of 12 subjects with HIV-DL had Carr scores
consistent with HIV-lipodystrophy. In contrast, 2 of our 12
subjects who had HIV infection without dyslipidemia met clini-
cal or Carr criteria for HIV-lipodystrophy. Our results are
consistent with data from previous studies, which found that
insulin resistance was associated with HIV-lipodystrophy (2,
45, 48). Therefore, the results from the present study support
and expand the findings from previous studies and suggest that
dyslipidemia alone may be an important marker of multiorgan
(skeletal muscle, liver, and adipose tissue) insulin resistance.

Intrahepatic lipid content was much greater in subjects with
HIV with dyslipidemia than in those with HIV without dys-
lipidemia and control subjects. The increase in intrahepatic
lipid is likely due to an increase in hepatic fatty acid availability
for TG production in conjunction with an inadequate compensatory
increase in hepatic fatty acid oxidation and triglyceride secretion.
Although postabsorptive FFA release rate into systemic plasma was the same in all three groups, total
daily FFA delivery to the liver was probably greater in those
with HIV with dyslipidemia than in those without dyslipidemia
because of impaired insulin-mediated suppression of lipolysis
of subcutaneous adipose tissue triglycerides and increased
release of FFA directly into the portal circulation from ex-
panded visceral fat stores. In addition, Hellerstein et al. (21)
found that HIV infection increases de novo hepatic lipogenesis.
It is not known whether hepatic fatty acid oxidation is impaired
in patients with HIV-DL; whole body fat oxidation rates have
been reported to be both decreased (25) and increased (38) in
subjects with HIV-DL compared with healthy volunteers. We
(35) have previously found that hepatic VLDL-triglyceride
secretion is greater in subjects with HIV-DL than healthy
volunteers, suggesting that the accumulation of intrahepatic fat
is caused by an increase in hepatic triglyceride production that
exceeds the liver’s ability to export triglyceride as VLDL.

Our results suggest that circulating adipokines are involved
in the pathogenesis of insulin resistance in liver and skeletal
muscle in patients with HIV-DL. Adiponectin, which is the
most abundant protein secreted by adipocytes, increases fatty
acid oxidation (16) and insulin-mediated suppression of he-
patic glucose production (4). Infusion of IL-6 increases lipo-
lytic rates in humans (44) and blunts insulin action in liver and
skeletal muscle in mice (23). Low plasma adiponectin concen-
tration is associated with insulin-resistant glucose metabolism
in subjects who do not have HIV infection (47). In addition, the
results of a study conducted in men with HIV infection found
decreased plasma adiponectin concentration and increased IL-6
concentration correlated with insulin resistance, assessed by
HOMA-IR and quantitative insulin sensitivity check index
(QUICKI) (46). In our study, plasma adiponectin concentra-
tions were inversely correlated, and plasma IL-6 concentrations were directly correlated, with insulin-mediated suppression of endogenous glucose production and stimulation of glucose disposal in men with HIV-DL. Additional studies are needed to determine whether these correlations represent a simple association or a true causal relationship.

The heterogeneity of HAART regimens, and prior HAART exposure, in patients with HIV-DL limits our ability to evaluate medication-specific metabolic effects. Many patients with HIV infection require changes in HAART regimen due to virologic failure and drug-related side effects. Therefore, the diverse HAART regimens of our subjects reflects the current clinical practice for many HIV-infected people. Addition of some, but not all, PIs to HAART regimens can increase insulin resistance in patients with HIV infection (48). However, insulin action was not different in subjects with HIV without dyslipidemia who were receiving and not receiving PI therapy. It is possible that the addition of PI to the HAART regimen of these patients worsened their insulin sensitivity, but this impairment could not be detected by the cross-sectional design of our study.

The results from this study suggest that dyslipidemia is a marker of hepatic, skeletal muscle, and adipose tissue insulin resistance in patients with HIV infection. These findings could have important clinical implications because insulin resistance is a major risk factor for type 2 diabetes and CHD (32, 36). Therefore, early identification of insulin resistance could lead to earlier and more effective intervention strategies to delay or prevent the development of type 2 diabetes and CHD in HIV-infected patients.

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