Exercise and Vitamin E Intake Are Independently Associated with Metabolic Abnormalities in Human Immunodeficiency Virus–Positive Subjects: A Cross-Sectional Study

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We investigated the relationship among habitual exercise, diet, and the presence of metabolic abnormalities (body fat redistribution, dyslipidemia, and insulin resistance) in a cross-sectional study of 120 human immunodeficiency virus (HIV)–infected subjects with use of bivariate and multivariate regression-analysis models. Total and aerobic exercise were significantly and negatively associated with fasting plasma triglyceride levels in the entire sample and in the fat redistribution group. Inverse associations between total or aerobic exercise and insulin resistance were suggestive but did not achieve statistical significance. Diastolic blood pressure was significantly and inversely associated with supplemental or total but not habitual dietary intake of vitamin E.

In conclusion, exercise and vitamin E intake were independently and negatively associated with several phenotypic manifestations of HIV-associated metabolic syndrome, whereas other macro- or micronutrients did not have comparable significance.

HIV-associated metabolic syndrome, which is characterized by body fat redistribution (FR), dyslipidemia, and insulin resistance (IR), is frequently observed in patients treated with HAART that contains protease inhibitors (PIs) but can also be found in PI- and even treatment-naive patients [1–5]. The underlying mechanisms are still unknown [1, 6, 7]. However, the mere presence of metabolic abnormalities suggests an increased risk for developing atherosclerotic cardiovascular disease in HIV-infected patients [1, 8–11], particularly given the prolonged duration of survival associated with HAART [12, 13]. The optimal treatment options for this syndrome have not been established, and, because diet and exercise improve the metabolic profile of healthy individuals [14–22], it is important to also explore their potentially beneficial effects in HIV-positive patients.

Four small interventional studies have investigated the effect of exercise regimens consisting of various durations and contents [23–26], but no observational study has specifically explored the relationship between habitual exercise and HIV metabolic syndrome. Such a study could provide important insights regarding the beneficial effects of exercise and could contribute to the selection of an optimal exercise regimen to be then tested by an interventional study.
Two previous cross-sectional studies found no significant relationship between macronutrient intake and various metabolic parameters in HIV-infected individuals [27, 28]; however, Haidig et al. [28] reported that the ratio of polyunsaturated fat to saturated fat (P:S) was positively associated with IR, whereas dietary fiber was inversely associated with IR in the FR group. Other dietary factors known to influence the metabolic syndrome in HIV-negative subjects—including monounsaturated and omega 3 fats, trans fatty acids, fiber, folate, and vitamin E [15–18, 29–32]—have not been evaluated in the context of HIV metabolic syndrome. Finally, with the exception of a recent case report [33], no previous study has jointly investigated the influence of diet and exercise on the metabolic abnormalities of HIV-positive subjects. To provide additional insights into the relationship among diet, exercise, and phenotypic manifestations of HIV metabolic syndrome, we analyzed data obtained in the context of an ongoing cross-sectional study at the Beth Israel Deaconess Medical Center (Boston, MA).

PATIENTS AND METHODS

Study cohort. The study evaluated 120 HIV-infected subjects during a single outpatient visit to the General Clinical Research Center. Inclusion criteria were age ≥16 years, documented HIV infection, and ≥6 months of cumulative exposure to any antiretroviral regimen. Methods used for FR evaluation have been explained in detail elsewhere [34]. The Institutional Review Board at Beth Israel Deaconess Medical Center approved the study, and all subjects gave informed consent before participation.

Diet evaluation. We used a previously validated self-administered food frequency questionnaire (FFQ) (Block 98 revision of Block/NCI Health Habits and History Questionnaire; BDDS) that is appropriate for white, black, and Hispanic adults [35–38]. Respondent level estimates of energy, macronutrients, and food-group consumption for the year preceding the study were obtained from the analysis of 113 completed questionnaires.

Exercise evaluation. Current exercise was evaluated using 3 multiple-choice questions regarding the type and intensity of exercise (1, slight; 2, moderate; and 3, heavy), as described elsewhere [39] (i.e., 1, walking on level ground/swimming; 2, running, aerobic classes, or use of cardiovascular machines, treadmill, or stationary bike; and 3, weight training), exercise frequency (from 0 to ≥7 sessions/week), and session duration (<15, 15–29, 30–59, 60–89, or ≥90 min). Cumulative indexes for either aerobic or total (aerobic and/or resistance) exercise were calculated as number of sessions per week × duration (min) per session × exercise intensity. All subjects completed the exercise questionnaire.

Laboratory data. We measured fasting serum glucose level, insulin level, and lipid profile, and IR was estimated as described elsewhere [34, 40–44]. A complete metabolic profile was available for 116 subjects.

Radiological studies. Body composition was measured in all subjects using dual-energy x-ray absorptiometry scans (Hologic QDR-2000 version 5.73A; Hologic) [45, 46]. Visceral and subcutaneous abdominal fat was measured in 113 subjects using single-slice CT scans at the L4 level [47–50].

Data analysis. We used Kruskal-Wallis tests followed by post hoc (Mann-Whitney) analysis for comparisons of continuous variables among the 4 FR subgroups (non-FR, fat accumulation [FA], fat wasting [FW], and mixed FR) (SPSS version 8.0; SPSS). χ² tests followed by post hoc (Fisher’s exact) analysis were used for categorical variables. We also compared the entire FR and the non-FR subgroups using independent Student’s t or Mann-Whitney tests for continuous variables and χ² tests for categorical variables.

We then investigated potential associations among exercise, dietary intake, and several aspects of HIV metabolic syndrome (expressed as continuous variables) using bivariate and multivariate linear regression analyses with adjustment for consecutively introduced variables, including age, sex, total amount of tobacco use (packs per week × years), amount of current alcohol use (drinks per week), energy intake, CD4 cell count, duration of exposure to HIV treatment, body mass index (BMI), waist-to-hip ratio (WHR), and/or body composition, as indicated in the respective tables. Variables were included if they were found to be statistically significant in univariate analysis or if they were considered to be associated with HIV metabolic syndrome. Further adjusting our analysis for treatment with oral antihyperglycemic agents (2 subjects) and/or hypolipidemic treatment (17 subjects) did not significantly change the results. We conducted similar analyses in the entire HIV group, then in the non-FR and FR groups, followed by analyses in each FR subgroup separately. We conducted logarithmic transformation of variables that were not normally distributed (as indicated in the tables). All tests reported herein are 2-tailed.

Bonferroni’s correction was used to adjust for multiple comparisons. Thus, a P value of .05–.008 was considered to be suggestive of statistical significance, and P<.008 was considered to be statistically significant for all analyses.

RESULTS

Fifty-one subjects (43%) did not have any evidence of FR, whereas 17 subjects (14%) had regional FA, 23 (19%) had peripheral FW, and 29 (24%) had a mixed FR profile (table 1). Most subjects were male (89%) and white (76%). The mixed-FR group was the oldest, whereas the FA group included the highest percentage of women (29%), and there were no significant differences in ethnicity among the 4 FR groups (table 1). Eighty-two subjects (68%) were current or past smokers
Table 1. Baseline characteristics of the study group.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All</th>
<th>Fat redistribution</th>
<th>Fat accumulation</th>
<th>Mixed-FR group</th>
<th>FW group</th>
<th>Overall P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 120)</td>
<td>(n = 51)</td>
<td>(n = 69)</td>
<td>(n = 17)</td>
<td>(n = 29)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>Age, years</td>
<td>43.7 ± 8.0</td>
<td>41.9 ± 7.6</td>
<td>45.0 ± 8.1</td>
<td>43.0 ± 7.4</td>
<td>47.0 ± 8.9</td>
<td>44.0 ± 7.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>107</td>
<td>48</td>
<td>59</td>
<td>12</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>3</td>
<td>10</td>
<td>5</td>
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<tr>
<td>White</td>
<td>104</td>
<td>43</td>
<td>61</td>
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</tr>
<tr>
<td>Black</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.4 ± 3.5</td>
<td>23.9 ± 2.4</td>
<td>24.8 ± 4.0</td>
<td>28.3 ± 4.8</td>
<td>24.7 ± 2.9</td>
<td>22.3 ± 2.6</td>
</tr>
<tr>
<td>Waist: hip ratio</td>
<td>0.97 ± 0.07</td>
<td>0.94 ± 0.05</td>
<td>0.99 ± 0.07</td>
<td>0.99 ± 0.07</td>
<td>1.02 ± 0.07</td>
<td>0.94 ± 0.04</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>14.9 ± 7.8</td>
<td>14.3 ± 5.3</td>
<td>15.3 ± 9.3</td>
<td>24.5 ± 10.4</td>
<td>15.3 ± 6.9</td>
<td>8.4 ± 3.6</td>
</tr>
<tr>
<td>Total fat mass, %</td>
<td>19.5 ± 8.2</td>
<td>19.4 ± 6.3</td>
<td>19.6 ± 9.3</td>
<td>28.6 ± 8.4</td>
<td>20.2 ± 7.6</td>
<td>12.1 ± 4.8</td>
</tr>
<tr>
<td>Subcutaneous abdominal fat, cm²</td>
<td>125.4 ± 93.2</td>
<td>122.9 ± 66.2</td>
<td>127.4 ± 110.6</td>
<td>247.1 ± 105.4</td>
<td>118.5 ± 90.1</td>
<td>47.1 ± 33.0</td>
</tr>
<tr>
<td>Visceral abdominal fat, cm²</td>
<td>122.9 ± 68.1</td>
<td>98.6 ± 41.8</td>
<td>142.2 ± 78.3</td>
<td>181.3 ± 81.1</td>
<td>159.8 ± 74.3</td>
<td>90.8 ± 52.7</td>
</tr>
<tr>
<td>HIV infection and antiretroviral therapy</td>
<td>11,804 ± 42,568</td>
<td>4514 ± 11,808</td>
<td>17,301 ± 55,003</td>
<td>3283 ± 11,370</td>
<td>16,032 ± 50,724</td>
<td>30,171 ± 76,982</td>
</tr>
<tr>
<td>CD4 cell count, cells/mm³</td>
<td>484 ± 283</td>
<td>486 ± 250</td>
<td>483 ± 308</td>
<td>598 ± 403</td>
<td>423 ± 252</td>
<td>477 ± 286</td>
</tr>
<tr>
<td>Total PI use, months</td>
<td>37 ± 25</td>
<td>31 ± 26</td>
<td>41 ± 24</td>
<td>37 ± 25</td>
<td>42 ± 19</td>
<td>44 ± 28</td>
</tr>
<tr>
<td>Total NRTI use, months</td>
<td>119 ± 57</td>
<td>96 ± 57</td>
<td>136 ± 51</td>
<td>104 ± 52</td>
<td>148 ± 45</td>
<td>146 ± 49</td>
</tr>
<tr>
<td>Total NNRTI use, months</td>
<td>12 ± 12</td>
<td>11 ± 12</td>
<td>13 ± 13</td>
<td>14 ± 15</td>
<td>14 ± 13</td>
<td>12 ± 11</td>
</tr>
<tr>
<td>Metabolic variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td>129/74</td>
<td>126/72</td>
<td>130/75</td>
<td>127/72</td>
<td>129/75</td>
<td>135/76</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>75 ± 11</td>
<td>75 ± 13</td>
<td>74 ± 10</td>
<td>77 ± 10</td>
<td>74 ± 12</td>
<td>73 ± 11</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>215 ± 65</td>
<td>212 ± 56</td>
<td>217 ± 71</td>
<td>210 ± 47</td>
<td>226 ± 93</td>
<td>211 ± 55</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>118 ± 42</td>
<td>125 ± 44</td>
<td>113 ± 40</td>
<td>122 ± 40</td>
<td>104 ± 45</td>
<td>116 ± 33</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>36 ± 11</td>
<td>39 ± 11</td>
<td>33 ± 11</td>
<td>42 ± 13</td>
<td>31 ± 9</td>
<td>30 ± 9</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>321 ± 363</td>
<td>219 ± 157</td>
<td>396 ± 448</td>
<td>231 ± 192</td>
<td>531 ± 619</td>
<td>353 ± 234</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>92.3 ± 32.6</td>
<td>84.8 ± 9.0</td>
<td>97.9 ± 40.3</td>
<td>115.2 ± 53.3</td>
<td>96.9 ± 43.1</td>
<td>96.6 ± 15.1</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>22.3 ± 23.0</td>
<td>12.4 ± 6.0</td>
<td>29.6 ± 27.9</td>
<td>30.6 ± 24.3</td>
<td>31.5 ± 28.4</td>
<td>26.4 ± 30.3</td>
</tr>
<tr>
<td>Insulin resistance, HOMA</td>
<td>5.7 ± 7.9</td>
<td>2.5 ± 1.3</td>
<td>8.1 ± 9.8</td>
<td>10.1 ± 10.7</td>
<td>8.8 ± 11.4</td>
<td>5.6 ± 5.9</td>
</tr>
</tbody>
</table>

**NOTE.** Data are mean ± SD, unless otherwise indicated. BMI, body mass index; FA, fat accumulation; FR, fat redistribution; FW, fat wasting; HDL, high-density lipoprotein; HOMA, homeostasis model; LDL, low-density lipoprotein; NRTI, nonnucleoside reverse-transcriptase inhibitor; NNRTI, nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

* .008 < P < .05 vs. non-FR group.
* .008 < P < .05 vs. mixed-FR group.
* .008 < P < .05 vs. FA group.

**P < .008 vs. FA group.**

**P < .008 vs. mixed-FR group.**
reported current alcohol drinking (4.6 ± 4.9 drinks per week), without significant differences among the FR groups. We found significant body composition differences among groups, with the FW group having significantly less total and abdominal fat than the FA or mixed FR groups (table 1).

There was no significant difference in the current CD4 cell count or virus load among the FR groups (table 1). Most patients had been exposed to PI (87%), nucleoside reverse-transcriptase inhibitor (NRTI) (98%), and nonnucleoside reverse-transcriptase inhibitor (NNRTI) (72%) therapy. The FW and mixed-FR groups had a significantly longer exposure to both PI and NRTI treatment than did the non-FR group, despite the fact that the duration since diagnosis of HIV infection was similar in all FR groups. At the time of evaluation, 62%, 97%, and 42% of subjects were receiving PI, NRTI, and NNRTI therapy, respectively, and 59% were receiving at least 1 PI and 1 NRTI simultaneously.

Fasting insulin levels and the IR index, estimated using the homeostasis model (HOMA), were significantly higher in the FA and mixed-FR groups, whereas high-density lipoprotein (HDL) cholesterol levels were higher in the FA and non-FR groups. The highest triglyceride (TG) levels were detected in the mixed FR group (table 1).

Exercise evaluation. The percentage of subjects performing different types of exercise was not different among the FR groups, although the mixed-FR group reported less frequent and shorter exercise sessions, resulting in lower exercise indexes compared with other groups (table 2). The highest exercise indexes were observed in the FW group.

Exercise and dyslipidemia. Bivariate and multivariate linear regression analyses of the entire study sample, with and without adjustment for age, sex, tobacco and alcohol use, WHR, fat percentage, presence of FR, current CD4, and duration of PI, NRTI, or NNRTI use, showed significant negative associations between fasting TG levels and the total exercise index (standardized β coefficient [std β] = −0.28; \( P = .004 \); table 3). These associations were even stronger when the entire FR group was considered separately (std β = −0.36; \( P = .008 \)) but were not significant in the non-FR group. Separate analyses for each of the 3 FR groups revealed negative associations between total exercise and TGs in the mixed-FR group (std β = −0.39; \( P = .09 \)) and the FW group (std β = −0.27; \( P = .24 \)) that was of similar strength as the ones shown in the entire sample, but these associations did not achieve statistical significance at the conventional \( P = .05 \) level, probably because of the small sample sizes. Similar results were detected when the aerobic exercise index was used instead of the total exercise index in the analysis. In contrast to TGs, no relationship was found between total or aerobic exercise and fasting low-density lipoprotein (LDL), HDL, or total cholesterol levels in the entire group or in any of the FR subgroups.

Exercise and insulin resistance. Similar bivariate and multivariate regression analysis models suggested an inverse relationship between total exercise and IR, but this association was borderline significant in the entire sample (std β = −0.20; \( P = .03 \); table 3) and in the FR group (std β = −0.26; \( P = .07 \)). FR subgroup analysis showed an equally strong, but not significant, association between total exercise and the HOMA-IR index in the FA group (std β = −0.38; \( P = .21 \)) and the FW group (std β = −0.30; \( P = .20 \)) but no association in the mixed-FR and non-FR groups. Negative borderline associations between aerobic exercise and IR were also suggested. Furthermore, the IR index tended to be associated with exercise session duration (std β = −0.21; \( P = .02 \)).

Exercise and body composition. Our analysis suggested a positive association between total exercise and lean body mass (LBM) in the entire sample and in the non-FR group (std β = 0.19 [\( P = .03 \)] and std β = 0.30 [\( P = .02 \)], respectively). An inverse association between total exercise and body fat percentage was also found in the non-FR group (std β = −0.29; \( P = .03 \)). As was expected, heart rate was negatively associated with total exercise in the entire sample and in the non-FR group (std β = −0.23 [\( P = .03 \)] and std β = −0.42 [\( P = .01 \)], respectively).

Dietary intake analysis. Subjects in each group reported a higher dietary fat intake than is recommended for the general population but a relatively lower carbohydrate percentage intake (table 2) [51]. Subjects in the FW group consumed the highest amount of daily calories; thus, they reported the highest amount of dietary (but not supplemental) vitamin E, folate, and fiber intake, whereas subjects in the FA group reported consuming the lowest percentage of fat, especially saturated and monounsaturated fat.

Dietary intake and insulin resistance. Bivariate and multivariate regression analysis models of the entire sample adjusting for age, sex, BMI, WHR, body fat percentage, energy intake, tobacco and alcohol use, CD4 cell count, and months of PI, NRTI, or NNRTI use suggested an inverse relationship between the total intake of vitamin E and IR (std β = −0.22; \( P = .04 \); table 4). However, these associations became nonsignificant after controlling for exercise, which indicates a potential confounding effect of exercise. Associations of similar strength were found in the FA and non-FR groups, but they were not statistically significant because of small sample sizes. Similar results were obtained when analyzing the supplemental, but not the habitual, dietary vitamin E intake.

We did not find any significant relationship among dietary energy, protein, carbohydrate, fat (total, saturated, monounsaturated, polyunsaturated, omega-3 fat, and trans fatty acids),
Similar associations were found in the FA and non-FR groups, but they were not statistically significant. Similar results were obtained when analyzing the supplemental, but not the habitual, dietary vitamin E intake.

**Dietary intake and dyslipidemia.** Using similar models, we found no significant relationships between any dietary components and fasting TG, LDL, HDL, or total cholesterol levels (table 4).
**Dietary intake and body composition.** Similar to the observed associations with diastolic blood pressure and insulin resistance, total intake of vitamin E was inversely associated with body fat percentage and subcutaneous abdominal fat (std $\beta = -0.29 \ [P = .003]$ and std $\beta = -0.33 \ [P = .004]$, respectively).

Finally, we explored whether exercise could interact with dietary variables in predicting levels of metabolic variables. No significant interactions between vitamin E and exercise, dietary fiber and exercise, or P:S fat ratio and exercise in relation to metabolic parameters were found.

**DISCUSSION**

Across the entire HIV-infected group, we found a significant independent negative association between fasting TG levels and habitual aerobic or combined aerobic and resistance training, and our data are suggestive of a negative relationship between exercise and insulin resistance. We also found a significant independent inverse relationship between vitamin E intake and diastolic blood pressure, body fat, and possibly insulin resistance. In contrast, no other dietary variables appear to play a role of comparable significance.

The inverse relationship between total or aerobic exercise and fasting TG levels reported here is in agreement with results from 2 previous interventional studies involving HIV-positive subjects [23, 24]. The effect of exercise on TG levels is possibly due to the increased lipoprotein lipase expression in muscle that is observed shortly after exercise [52–54]. This enzyme stimulates the release of free fatty acids (FFAs) from plasma lipoproteins, which are used by the muscle to replenish intramuscular TG deposits, thus lowering serum TG levels [52–54].

In contrast to the finding by Yarasheski et al. [23] that the increased muscle mass with a higher capacity to uptake and store plasma FFAs may have contributed to the improvement in TG levels observed with resistance training, we found that the inverse association between exercise and fasting TGs is independent of LBM (std $\beta = -0.33; \ P = .001$).

Our analysis suggests that an inverse relationship exists between total or aerobic exercise and IR in HIV-infected patients. Yarasheski et al. [23] found no significant change of fasting insulin levels in HIV-positive subjects doing resistance exercise, whereas Roubenoff et al. [33] reported a 52% decrease in the HOMA-IR index (from 29.23 to 14.05) in one subject with HIV-associated metabolic syndrome after 4 months of a low fat–high fiber diet and intense combined aerobic and resistance training. Of interest, the percentage decrease in IR in that case report [33] is within the 95% confidence limits predicted using the data from our observational study.

We found that total and supplemental (but not habitual dietary) vitamin E intake is inversely and independently associated with diastolic blood pressure. In a previous report, vitamin E supplementation (600 mg/day) in HIV-negative subjects with type 2 diabetes mellitus improved brachial artery reactivity [55], an effect that is possibly mediated through changes in the plasma reduced:oxidized glutathione ratio and oxygen free-radical levels, which generate an increase in the intracellular magnesium concentration and produce smooth-muscle relaxation, subsequently decreasing blood pressure [56–59]. However, the role of vitamin E on vascular reactivity in HIV-negative subjects remains controversial and needs to be further investigated.

In contrast to the findings by Hadigan et al. [28], which...
suggested that the dietary P:S fat ratio and fiber intake are strong independent predictors of hyperinsulinemia among HIV-positive patients with FR, we did not find a significant association between daily energy and macronutrient intake and any parameters of HIV-associated metabolic syndrome, even when we extended the analysis to factors that are known to influence the metabolic profile of HIV-negative subjects [15–18, 29–31], such as monounsaturated, polyunsaturated, omega 3 fats, and trans fatty acids, fiber, and folate. The divergence in the results of these 2 studies can be potentially explained by the different methodologies used. Specifically, we used the self-administered Block FFQ for dietary history versus the modified Burke diet history technique, and we used the HOMA-IR index to assess insulin resistance versus the insulin area under the curve (derived from an oral glucose challenge test) used in the other study. However, the HOMA-IR index correlates better with the reference standard euglycemic clamp technique [43, 44]. In addition, our sample size was larger, and our FR group reported a higher percentage of dietary fat and a higher P:S fat ratio. Finally, the wider range of insulin levels found in our study is more conducive toward the exploration of the potential role of the P:S fat ratio or fiber intake in modifying IR.}

Regarding the analysis of results, a potential nondifferential misclassification caused by random laboratory error or the effect of diurnal rhythms could theoretically be possible and would be expected to bias results toward the null and alter the P values toward nonsignificant values. However, all subjects were seen between 8 and 10 a.m., to minimize the effect of diurnal rhythms, and, even if misclassification occurred, it could not have led to an overestimation of the positive findings of the study. Conversely, an underestimation of the true association among diet, exercise, and metabolic variables might have occurred to the extent that nondifferential misclassification occurred. We eliminated differential misclassification by using blinded laboratory analysis. Although confounders were controlled through standard statistical procedures, residual confounding by other serum hormones or unmeasured factors remains a potential possibility. However, the validity of our analyses is supported by the demonstration of the negative associations between exercise and heart rate and the positive associations between exercise and LBMI.

We acknowledge that patients who developed FR may have changed their diet to improve the body shape changes, and reporting bias remains a possibility to the extent that subjects may report the diet that they think they should be eating. However, this was minimized, because no specific knowledge or study hypothesis on the potential effects of dietary factors on FR was available to study subjects at the time that the study was conducted. In addition, the food questionnaire asked specific questions about vitamin E and C, but it may not have assessed the other micronutrients as reliably; thus, results with respect to other micronutrients should be interpreted with caution. Finally, we recognize that our findings may not be directly relevant to all ethnic groups, given that the majority of our subjects were white (76%).

In conclusion, we found that exercise is independently and inversely associated with fasting TG levels and possibly insulin resistance, whereas vitamin E intake is inversely associated with diastolic blood pressure in HIV-positive subjects. The cross-sectional nature of the study limits determinations of temporality or causality. Therefore, future cohort and interventional studies to confirm these data and to assess the potential ther-

Table 4. Bivariate and multivariate linear regression analyses of daily total vitamin E intake as a predictor for metabolic variables in the study sample.

<table>
<thead>
<tr>
<th>Metabolic variable</th>
<th>β</th>
<th>β1</th>
<th>β2</th>
<th>β3</th>
<th>β4</th>
<th>β5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP, mmHg</td>
<td>−0.03</td>
<td>0.00</td>
<td>−0.06</td>
<td>−0.12</td>
<td>−0.12</td>
<td>−0.12</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>−0.25a</td>
<td>−0.25a</td>
<td>−0.31b</td>
<td>−0.29b</td>
<td>−0.33b</td>
<td>−0.30abc</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>−0.08</td>
<td>−0.07</td>
<td>−0.06</td>
<td>−0.05</td>
<td>−0.06</td>
<td>−0.06</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>−0.18</td>
<td>−0.16</td>
<td>−0.18</td>
<td>−0.16</td>
<td>−0.11</td>
<td>−0.17</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>0.04</td>
<td>0.02</td>
<td>−0.04</td>
<td>0.06</td>
<td>0.06</td>
<td>0.03</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>−0.06</td>
<td>−0.05</td>
<td>−0.02</td>
<td>−0.09</td>
<td>−0.15</td>
<td>−0.11</td>
</tr>
<tr>
<td>Insulin resistance, HOMA</td>
<td>−0.12</td>
<td>−0.08</td>
<td>−0.11</td>
<td>−0.19a</td>
<td>−0.23b</td>
<td>−0.22a</td>
</tr>
</tbody>
</table>

**NOTE.** β, Bivariate standardized β coefficient; Δ1, standardized Δ coefficient adjusted for age and sex; β2, adjusted for age, sex, tobacco and alcohol use, and BMI; β3, adjusted for age, sex, tobacco and alcohol use, BMI, fat percentage, and waist-to-hip ratio (WHR); β4, adjusted for age, sex tobacco and alcohol use, BMI, fat percentage, WHR, current CD4 cell count, and months of protease inhibitor (PI), nucleoside reverse-transcriptase inhibitor (NRTI), nonnucleoside reverse-transcriptase inhibitor (NNRTI) use, β5, adjusted for age, sex, tobacco and alcohol use, BMI, fat percentage, WHR, CD4 cell count, months of PI, NRTI, NNRTI use, and daily energy intake; BP, blood pressure; HDL, high-density lipoprotein; HOMA, homeostasis model; LDL, low-density lipoprotein.

a. P < .001.
b. P < .008.
c. P < .001.
d. Log10 transformed before analysis.
apeutic efficacy of exercise and diet in HIV-associated metabolic syndrome are needed.

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References