Gradual increases in dyslipidemia among male patients with human immunodeficiency virus primarily treated with tenofovir plus lamivudine plus efavirenz: a 3-year follow-up study

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Research

Keywords: human immunodeficiency virus (HIV), antiretroviral therapy (ART), lipid metabolism parameter, uric acid, dynamic change, long-term

DOI: https://doi.org/10.21203/rs.3.rs-238801/v1

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Abstract

Introduction: Since the development of antiretroviral therapy (ART) with TDF plus 3TC plus EFV, this specific regimen has not been studied enough with long-term lipid and uric monitoring.

Methods: A prospective follow-up cohort study was performed. Sixty-one treatment-naive male patients with HIV were divided into three groups based on their baseline CD4+ T cell count (26, 12, and 23 patients in the <200, 200 to 350, and >350 groups, respectively). The lipid and purine metabolism parameters of the patients over 144 weeks were analyzed.

Result: TG, TC, LDL-c and HDL-c levels all gradually increased over 144 weeks, but the increases in TC levels and HDL-c levels were significant (P=0.001, 0.000, respectively). Moreover, the percentages of hypercholesterolemia, hyper LDL cholesterol and hypertriglyceridemia all showed gradual and nonsignificant increases; the percentage of low HDL cholesterol showed a gradual and significant decrease (P=0.0007). Furthermore, the lower the baseline CD4+ T lymphocyte counts were, the higher the TG levels were and the lower the TC, LDL-c and HDL-c levels were. However, only baseline LDL-c levels differed significantly between the three groups (P=0.0457). Although the UA level and the percentages of hyperuricemia gradually increased over 144 weeks, there was no significant difference between the different follow-up time point groups or between the three CD4+ T cell count groups (all P>0.05). Further analyses revealed that the main factors contributing to lipid metabolism were age, anthropometric parameters and follow-up weeks, and virus load was the main factor contributing to uric acid levels.

Conclusions: These findings provide a reference for clinicians to monitor lipid metabolism parameters closely during long-term ART with the TDF plus 3TC plus EFV regimen.

Introduction

In recent years, the numbers of patients with human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) have sharply increased. By the end of 2019, approximately 38 million people worldwide lived with HIV, and 33 million people died of HIV-related diseases [1]. At the end of October 2019, a total of 958,000 patients in China were living with HIV [2, 3]. At the end of September 2018, a total of 262,000 patients died of HIV-related diseases in China [2, 3].

The most effective treatment for AIDS is antiretroviral therapy, which can prolong life expectancy and improve quality of life [4, 5]. When a patient's CD4+ T cell count reaches more than 350/mm3 and the viral load reaches undetectable levels within the first year of starting treatment, AIDS patients are predicted to have a normal life expectancy [4, 5]. The cumulative survival rates of AIDS patients have increased markedly [6-8]. As of 2017, 20.9 million patients with HIV had received antiretroviral treatment worldwide. However, metabolic abnormalities, cardiovascular risk factors, and osteoporosis have become important factors affecting the prognosis and quality of life of AIDS patients [9-12].

HIV infection itself and antiretroviral therapy (ART) treatment drugs can cause dyslipidemia. However, as a first-line ART program launched since the National Twelfth Five-Year Plan in China, the tenofovir (TDF) plus lamivudine (3TC) plus efavirenz (EFV) regimen has a weaker effect on lipid metabolism. Our previous study showed that newly diagnosed male AIDS patients had decreased total cholesterol (TC) levels, uric acid (UA) levels [13,14], and high-density lipoprotein cholesterol (HDL-c) levels as well as increased triglyceride (TG) levels, especially patients with CD4+ counts <200/µl. The dyslipidemia and decreased UA levels gradually returned to normal 4 weeks after initial ART with the TDF plus 3TC plus EFV regimen [13,14]. This specific regimen has not been studied enough using long-term lipid and uric monitoring, which is the focus of the current study.

Patients And Methods

Study population

A prospective cohort study was conducted on sixty-one male patients with HIV who were treatment-naive at the Public and Health Clinic Centre of Chengdu from October 1, 2012, to December 31, 2017. Among them, the first 50 cases have been described in the literature [13-15].
The following exclusion criteria were used in this study: patients with acute infections; patients with opportunistic infections or AIDS-related malignant tumors at the time of enrollment; patients with opportunistic infection occurring within 3 months before enrollment and still in unstable condition within 2 weeks before enrollment; patients with hemoglobin <9g/dL, white blood cell count <2000/µL, neutrophil count <1000/µL, platelet count <75000/µL, serum creatinine >1.5-fold upper limit of the normal value (ULN), aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3-fold ULN, total bilirubin >2-fold ULN, serum creatine phosphokinase >2-fold ULN, or creatinine clearance rate <60 mL/min; women who were pregnant or lactating; current drug users; patients with severe mental or neurological diseases; patients with a history of alcoholism; and patients with severe digestive tract ulcers.

AIDS, dyslipidemia and hyperacidemia diagnostic criteria were applied according to the corresponding guidelines. [16-18]. According to guidelines, the cutoff values for determining hypercholesterolemia, hyper-low-density lipoprotein cholesterol, hypo-high-density lipoprotein cholesterol, hypertriglyceridemia and hyperuricemia were as follows: total cholesterol (TC) ≤5.18 mmol/L, low-density lipoprotein cholesterol (LDL-c) ≤3.37 mmol/L, high-density lipoprotein cholesterol (HDL-c) <1.0 mmol/L, triglyceride ≤1.7 mmol/L, and uric acid (UA) ≤420 μmol/L, respectively.

The participants were divided into three groups according to their baseline CD4 T cell counts: there were 26, 12, and 23 patients in the <200, from 200 to 350 and >350 cells/µl groups, respectively.

Measurement of anthropometric parameters

The subjects fasted overnight for at least 12 hours. At 8:00 am the next day after emptying stool and urine, anthropometric parameters, including height, body weight (BW), body fat weight, body nonfat weight, body mass index (BMI) and body fat percentage, were measured by specially trained researchers using a body fat measuring instrument.

Detection of laboratory indicators

The subjects fasted overnight for at least 12 hours. At 8:00 am the next day, the venous blood of those patients was drawn to measure TC, LDL-c, HDL-c, TG, UA, HIV viral nucleic acid (HIVRNA), and T lymphocyte subsets.

TC, TG, HDL-c, LDL-c and UA levels were measured by the enzymatic method of an automatic biochemical analyzer purchased from Zhejiang Eastern European Biological Products Company. HIVRNA was detected by fluorescent quantitative PCR; T lymphocyte subsets (including CD3+ count, CD4+ count, CD8+ count, CD3+%, CD4+%, CD8+%) were measured by flow cytometry using a Beckman flow cytometer.

The follow-up time points were 0, 4, 8, 12, 24, 36, 48, 72, 84, 96, 108, 120, 132, and 144 weeks after patients underwent ART with the TDF plus 3TC plus EFV regimen. UA levels were measured at each follow-up time point, and TC, LDL-c, HDL-c and TG levels were detected at 0, 24, 48, 96, 120, and 144 weeks.

Databases were established according to the needs of the research by two researchers simultaneously collecting and entering data. Approximately 30% of the data were randomly selected by the researchers to assess data integrity, authenticity, and accuracy.

Patient and public involvement

Patients and the public were involved in the development of the research question or in the design of the study. Patients received oral and written information about this study; however, they were not involved in the recruitment and implementation of the study. In addition, the burden of the intervention was assessed by the patients themselves. After signing an informed consent form by the participants, they were assessed for eligibility prior to data collection.

Statistical methods

The Statistical Package for the Social Sciences software version 17.0 (IBM Inc., Armonk, NY, USA) and GraphPad Prism 8 (GraphPad) software were used for statistical analysis. TC, LDL-c, HDL-c, TG and UA levels normally distributed, and statistical analysis was conducted directly. Nonnormally distributed HIVRNA levels were subjected to natural logarithmic transformation before statistical analysis. Quantitative data were expressed as χ±SD, and categorical data were expressed as rates or
percentages. One-way ANOVA was used to compare metabolism parameters from baseline to 144 weeks, and a paired t-test was used to compare metabolism parameters between baseline and some follow-up time points. The Kruskal-Wallis H (K) test for K independent samples was used to compare the percentage of dyslipidemia and hyperuricemia from baseline to 144 weeks. The Mann-Whitney test for two independent samples was used to compare the percentage of dyslipidemia and hyperuricemia between baseline and some follow-up time points. One-way ANOVA was used to compare metabolism parameters between the three different CD4+ T cell count groups at the same time point. Two-way ANOVA was used to compare metabolism parameters between the three different CD4+ T cell count groups from baseline to 144 weeks. A p value <0.05 was considered statistically significant.

Ethical consideration

The study was approved by the hospital ethics committee of the Public and Health Clinic Centre of Chengdu. All patients gave written informed consent.

Results

Baseline conditions

Sixty-one treatment-naive male patients with HIV in the Public and Health Clinic Centre of Chengdu from October 1, 2012, to December 31, 2017, were divided into three groups according to their baseline CD4+ T cell count: there were 26, 12, and 23 patients in the <200, 200 to 350, and >350 cell/µl groups, respectively. There were 42 cases of infection through homosexual contact, 13 cases of infection through heterosexual contact and 5 cases involving both types of sexual contact. The general information, baseline immunity and virological indicators, and lipid metabolism parameters of 61 patients are shown in Table 1.

Effectiveness of ART with the TDF plus 3TC plus EFV regimen

In 61 patients, the average CD4+ T cell count (Figure 1A) gradually increased from 319.80 cell/µl at baseline to 464.85 cell/µl at 96 weeks after ART, and the average viral load (Figure 1B) decreased rapidly from 49846.32 IU/ml at baseline to undetectable levels (measured by a high-precision detection method) at 72 weeks. The percentage of viral load reaching undetectable levels (Figure 1C) ranged from 21.31% at 12 weeks to 100.00% at 72 weeks.

Long-term dynamic changes in anthropometric parameters after treatment with TDF+3TC+EFV

The body weight (Figure 2A) and body nonfat weight (Figure 2B) of patients did not change significantly over the 144 weeks (all P>0.05). The body mass index (Figure 2C), body fat weight (Figure 2D) and body fat percentage (Figure 2E) of patients gradually increased over 144 weeks (all P<0.05), and the increments were 0.95 kg/m², 2.7 kg, and 4.31%, respectively; body fat weight and body fat percentage, in particular, showed considerable increases.

Long-term dynamic changes in lipid and purine metabolism parameters after treatment with TDF+3TC+EFV

The average increase is

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The average rate of increase, respectively

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The average increase is

The average rate of increase, respectively

No significant changes in 144 weeks

144 no significant change in weeks

TC, LDL-c, HDL-c, TG and UA levels (Figure 3A, 3B, 3C, 3D and 5A) all gradually increased with prolonged ART, but the increases were small, and only the increases in TC levels (Figure 3A) and HDL-c levels (Figure 3C) were statistically significant (0, 24, 48, 96, 120, 144 weeks: 4.20 vs. 4.13, 4.43, 4.60, 4.44, 4.67 mmol/L; 1.12 vs. 1.19, 1.32, 1.36, 1.23, 1.30 mmol/L; F=4.382, 6.033, P=0.0007, 0.000, respectively). Compared with baseline, there were significant differences in TC levels at 96 and 144 weeks (Figure 3A) and significant differences in HDL-c levels at 48, 96 and 144 weeks (Figure 3C) (4.20 vs. 4.60 mmol/L, 4.20 vs. 4.67 mmol/L; 1.12 vs. 1.32 mmol/L, 1.12 vs. 1.36 mmol/L, 1.12 vs. 1.30 mmol/L; t=3.155, 2.175, 3.610, 5.189, 2.473, P=0.002, 0.0329, 0.0004, 0.0001, 0.0157, respectively). There were no significant differences in LDL-c (Figure 3B), TG (Figure 3D) or UA levels (Figure 5A) between different time points compared with baseline (all P>0.05).

The percentages of hypercholesterolemia (Figure 4A), hyper-low-density lipoprotein cholestrololemia (Figure 4B) and hypertriglyceridemia (Figure 4D) all gradually increased, but the increases were not significant (24.59 vs. 29.51, 24.59, 21.31, 25.00, 50.00%; 9.84 vs. 8.20, 8.20, 18.03, 25.00, 21.43%; 8.20 vs. 8.20, 9.84, 18.05, 10.00, 21.43%, χ²=5.351, 7.966, 5.408, P=0.375, 0.158, 0.368, respectively). In contrast, the percentage of hypo-high-density lipoprotein cholesterolemia (Figure 4C) gradually decreased with prolonged ART, and a significant difference was found from baseline to 144 weeks (Figure 4C) (36.07 vs. 18.03, 16.39, 9.84, 20.00, 7.14%, χ²=16.105, P=0.0007) and at 24, 48, 96, 144 weeks compared with baseline (Figure 4C) (36.07 vs. 18.03, 16.39, 9.84,
20.00, 7.14%, 36.07 vs. 18.03%, 36.07 vs. 16.39%, 36.07 vs. 9.84%, 36.07 vs. 7.14%; Z=-2.233, -2.460, -3.431, -2.102, P=0.026, 0.014, 0.001, 0.036, respectively). The percentage of hyperuricemia (Figure 5B) slightly decreased with the extension of the HAART treatment time, but this decrease was not significant (P>0.05).

Effect of baseline CD4+ T cell count on lipid and purine metabolic parameters after treatment with TDF+3TC+EFV

The lower the CD4+ T cell count at baseline was, the higher the TG levels (Figure 6D) and the lower the TC (Figure 6A), LDL-c (Figure 6B), HDL-c (Figure 6C) and UA levels were (Figure 7); moreover, these changes were maintained throughout the follow-up period after ART treatment. However, there was no significant difference in the change from baseline to 96 weeks between the three different CD4+ T cell count groups (all P>0.05). The difference of the LDL-c levels (Figure 6B) at baseline was significant between the three different CD4+ T cell count groups (2.22 vs. 2.70, 2.67 mmol/L, F=3.256, P=0.0457). TC levels (Figure 6A) and HDL-c levels (Figure 6C) all gradually increased along with prolonged ART regardless of the CD4+ T cell count at baseline.

The contributing factors of lipid and purine metabolic parameters

According to Spearman correlation analysis, nonalcoholic fatty liver disease, age, body weight, BMI, body fat weight, and body fat percentage were all positively correlated with TC, TG and LDL-c levels; body nonfat weight was positively correlated with LDL-c levels; and follow-up duration was positively correlated with TC and HDL-c levels. In contrast, nonalcoholic fatty liver disease, body weight, BMI, body fat weight, body fat percentage and body nonfat weight were all negatively correlated with HDL-c levels (Table 2). Based on multiple stepwise regression analysis, the factors that affected TC levels were body weight, age, body nonfat weight and follow-up duration; the factors that affected TG levels were body weight, body nonfat weight, BMI and age; the factors that affected HDL-c levels were BMI, CD3+CD4+ count and body weight; and the factors that affected LDL-c levels were BMI and follow-up duration (Table 3).

In addition, nonalcoholic fatty liver disease, body weight, body nonfat weight, CD3+CD4+ cell count and virus load were all positively correlated with UA levels, while age was negatively correlated with UA levels (Table 2). Based on multiple stepwise regression analysis, only virus load was a contributing factor for UA (Table 3).

Discussion

Currently, most of the literature focuses on the proportion of abnormal lipid metabolism in patients treated with ART. As reported in the literature, the incidence of dyslipidemia in HIV/AIDS patients is quite high in Asia, especially in some southeast Asian countries, such Thailand (34.93%) [19], Tanzania (more than 76%) [20], southern Ethiopia (82.3%) [21] and India (20-100%) [22-25]. It has also been reported that 10-60% of patients receiving ART treatment have hypercholesterolemia [8,26-29], 20-70% have hypertriglyceridemia [8,9,29,30], 35.1% have hyper-low-density lipoprotein cholesterolemia [29], and 20-68.5% have hypo-high-density lipoprotein cholesterol [9,29-32]. No study has used long-term lipid and uric monitoring with specific first-line ART regimens, especially the TDF+3TC+EFV regimen.

In this prospective cohort study, we aimed to identify the long-term dynamic characteristics of lipid and purine metabolism and to identify influencing factors after ART with the TDF+3TC+EFV regimen. To our knowledge, this prospective 3-year follow-up cohort study was the first to report the use of long-term lipid and uric monitoring to assess the efficacy of the TDF+3TC+EFV regimen, baseline CD4+ T cell count, age, anthropometric parameters, and immunological and virological indicators of lipid and purine metabolic parameters in male patients with HIV undergoing primary treatment. The results showed that in patients treated with the TDF+3TC+EFV regimen for 3 years, TC, LDL-c and HDL-c levels gradually increased, especially TC and HDL-c levels. TG levels first gradually decreased and then gradually increased. Moreover, the percentages of hypercholesterolemia, hyper-low-density lipoprotein cholesterol and hypertriglyceridemia all gradually increased, while the percentage of hypo-high-density lipoprotein cholesterol gradually decreased. This shows that in the early stage of ART treatment, disordered lipid metabolism was improved, especially hypo-high-density lipoprotein cholesterol. However, along with prolonged ART, the proportion of hyperlipidemia and hypertriglyceridemia gradually increased, especially hyper-low-density lipoprotein cholesterol and hypertriglyceridemia after 48 weeks and hypercholesterolemia after 120 weeks, which ranged from 9.84%, 8.2%, and 24.59% at baseline to 21.43%, 21.43%, and 50.00% at 144 weeks, respectively. According to Spearman correlation analysis and based on
multiple stepwise regression analysis, the contributing factors of lipid and purine metabolic parameters included age, anthropometric parameters, and immunological and virological indicators.

This alternate cause of early lipid and purine metabolism may be partially due to the changes in appetite and weight gain among patients who contracted AIDS after ART treatment. However, this study found that within 48 weeks after ART, all anthropometric parameters of those patients, including body weight, body fat weight, lean body weight, body fat percentage and BMI, did not increase. Body weight increased by 2.81 kg, and body fat weight increased by 2.74 kg from 48 to 144 weeks, but lean body weight did not increase over the 144 weeks.

This study was a cohort study with a follow-up time of 144 weeks. The proportion of patients with abnormal lipid metabolism during the whole study period was less than that reported in the literature. The reasons may be related to the younger age of patients in this cohort, the duration of follow-up was not too long, and the TDF+3TC+EFV regimen had little effect on metabolism. It is still necessary to expand the sample size, increase the number of female patients, extend the follow-up time and increase other ART regimens for further discussion.

A previous study found that a high CD4+ cell count was a risk factor for hypertriglyceridemia, while a CD4+ cell count less than 200 copies/mm$^3$ increased the risk of hypercholesterolemia [29]. Regardless of whether the initial treatment regimen was based on D4T, the risk of hyperlipidemia in HIV/AIDS patients aged 50 and above was significantly higher than that in young HIV/AIDS patients aged under 40[33]. In this prospective 3-year follow-up cohort study, the long-term effect of baseline CD4+ T lymphocyte count on lipid parameters was that the lower the baseline CD4+ T lymphocyte count was, the higher the TG levels were and the lower the TC, LDL-c and HDL-c levels were.

A previous study reported that among patients living with HIV for a mean duration of 17.4 years, 35.6% had ASCVD, and of those without ASCVD, 53% to 86% had intermediate or moderate-to-high 10-year ASCVD risk scores, cardiovascular risk factors including HIV, 31.9% had low high-density lipoprotein cholesterol levels, and 79.3% needed to receive statin therapy [34].

After comparisons between different time points over the 144 weeks and comparisons with baseline levels, no significant difference in UA levels was found. The lower the baseline CD4+ T cell count was, the higher the UA levels were, and these changes were maintained throughout the follow-up period after ART treatment; however, there was no statistical significance in the change from baseline to 144 weeks between the three different CD4+ T cell count groups. That is, the TDF+3TC+EFV regimen and CD4+ T cell count at baseline had no long-term dynamic effects on purine metabolism.

Conclusions

These findings provide a reference for the clinical use of long-term lipid and uric monitoring during long-term ART with the TDF plus 3TC plus EFV regimen.

Abbreviations

AIDS: Acquired immunodeficiency syndrome; ART: Antiretroviral therapy; BMI: body mass index; BW: body weight; EFV: Efavirenz; HDL-c: high-density lipoprotein cholesterol; HIV: Human immunodeficiency virus; HIVRNA: HIV viral nucleic acid; 3TC: Lamivudine; LDL-c: low-density lipoprotein cholesterol; TC: Total cholesterol; TDF: tenofovir; TG: Triglycerides; ULN: normal value; UA: uric acid.

Declarations

Ethics approval and consent to participate

The study was approved by the hospital ethics committee of the Public and Health Clinic Centre of Chengdu. All patients gave written informed consent.

Consent for publication

All authors read and approved the final manuscript, and gave written informed consent for publication.
Availability of data and material

All data, models, or code generated or used during the study are available from the first author by request: Dafeng Liu, E-mail: ldf312@126.com

Competing interests

The authors declare that they have no conflicts of interest to this study.

Funding

This research was supported by the Twelfth Five-Year Project on Tackling Key Problems of National Science and Technology (2012ZX10001-003), the Sichuan Province Health Commission (130430;17PJ070), and the Chengdu Municipal Health Commission (2019079).

Authors’ contributions

Concept and design: Dafeng Liu, Bennan Zhao, Xinyi Zhang, Feng jiao Gao, Jun Kang, Xue Zheng, Lijuan Lan, Yinsheng He; Data acquisition: Dafeng Liu, Bennan Zhao, Xinyi Zhang, Feng jiao Gao, Jun Kang, Xue Zheng, Lijuan Lan; data analysis and interpretation: Dafeng Liu, Bennan Zhao, Xinyi Zhang; Drafting the manuscript: Dafeng Liu, Bennan Zhao, Xinyi Zhang; administrative, technical, or material support: Dafeng Liu, Bennan Zhao, Xinyi Zhang; study supervision: Shenghua He.

Acknowledgments

We thank Dr. Lin Cai, Ruifeng Zhou, and Yin Wang (the Public and Health Clinic Centre of Chengdu, one ward of infectious disease department).

References

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Tables

Table 1. Baseline information of male patients with HIV (n=61)
<table>
<thead>
<tr>
<th>variable</th>
<th>χ±SD or cases</th>
<th>%</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>age [years]</td>
<td>32.05±8.38</td>
<td>20~58</td>
<td></td>
</tr>
<tr>
<td>gender [male]</td>
<td>61(100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infection duration (months)</td>
<td>11.16±1.19</td>
<td>1~86</td>
<td></td>
</tr>
<tr>
<td>T lymphocyte subsets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD3+ count (cells/ul)</td>
<td>1433.98±595.35</td>
<td>470~3074</td>
<td></td>
</tr>
<tr>
<td>CD3+CD4+ count (cells/ul)</td>
<td>313.87±118.473</td>
<td>54~499</td>
<td></td>
</tr>
<tr>
<td>CD3+CD4+ percentage (%)</td>
<td>19.78±6.83</td>
<td>1.40~43.40</td>
<td></td>
</tr>
<tr>
<td>CD3+CD8+ count (cells/ul)</td>
<td>1119.70±605.0</td>
<td>360~2456</td>
<td></td>
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<tr>
<td>CD3+CD8+ percentage (%)</td>
<td>69.97±13.80</td>
<td>36.13~97.20</td>
<td></td>
</tr>
<tr>
<td>*Virus load of HIVRNA</td>
<td>41772.77±10.38</td>
<td>895.00~505987.00</td>
<td></td>
</tr>
<tr>
<td>metabolic parameters</td>
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<tr>
<td>TG (mmol/L)</td>
<td>1.68±1.23</td>
<td>0.39~16.81</td>
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<tr>
<td>TC (mmol/L)</td>
<td>4.20±0.72</td>
<td>2.38~6.09</td>
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<tr>
<td>LDL-c (mmol/L)</td>
<td>2.61±0.68</td>
<td>0.92~4.71</td>
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<tr>
<td>HDL-c (mmol/L)</td>
<td>1.12±0.24</td>
<td>0.57~1.77</td>
<td></td>
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<tr>
<td>UA (μmol/L)</td>
<td>310.72±68.65</td>
<td>143~506</td>
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<tr>
<td>anthropometric parameters</td>
<td></td>
<td></td>
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<tr>
<td>Body weight (kg)</td>
<td>62.41±10.53</td>
<td>46~85</td>
<td></td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>21.38±2.82</td>
<td>16.80~28.20</td>
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<tr>
<td>Body fat percentage (%)</td>
<td>15.99±6.32</td>
<td>3~28.4</td>
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<tr>
<td>Body fat weight (kg)</td>
<td>10.40±5.33</td>
<td>1.4~22.10</td>
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<tr>
<td>Body nonfat weight (kg)</td>
<td>51.82±6.67</td>
<td>35.8~64.7</td>
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<td>Baseline body mass status</td>
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<tr>
<td>Body mass index&lt;18 kg/m²</td>
<td>3 (4.92)</td>
<td></td>
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</tr>
<tr>
<td>24Kg/m²≥Boby mass index≥18 kg/m²</td>
<td>49 (80.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index≥24 kg/m²</td>
<td>9 (14.75)</td>
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</tbody>
</table>

Note: Abbreviation: TG, triglyceride. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. UA, uric acid. *refers to logarithmic transformation before statistical analysis for nonnormally distributed data.

Table 2. Spearman correlation analysis between lipid metabolism parameters and age, anthropometric parameters, and immunological and virological indicators (n=61)
<table>
<thead>
<tr>
<th>Variable</th>
<th>TC (mmol/L)</th>
<th>TG (mmol/L)</th>
<th>HDL-c (mmol/L)</th>
<th>LDL-c (mmol/L)</th>
<th>UA (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>NAFLD[1=without, 2=with]</td>
<td>0.357</td>
<td>0.002</td>
<td>0.353</td>
<td>0.003</td>
<td>-0.255</td>
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<tr>
<td>Age (yr.)</td>
<td>0.304</td>
<td>&lt;0.0001</td>
<td>0.164</td>
<td>0.004</td>
<td>0.226</td>
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<tr>
<td>Body weight (kg)</td>
<td>0.243</td>
<td>0.013</td>
<td>0.241</td>
<td>0.014</td>
<td>-0.413</td>
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<tr>
<td>Body mass index (kg/m^2)</td>
<td>0.343</td>
<td>0.001</td>
<td>0.236</td>
<td>0.021</td>
<td>0.418</td>
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<td>Body fat percentage (%)</td>
<td>0.318</td>
<td>0.002</td>
<td>0.460</td>
<td>&lt;0.0001</td>
<td>-0.238</td>
</tr>
<tr>
<td>Body fat weight (kg)</td>
<td>0.312</td>
<td>0.002</td>
<td>0.390</td>
<td>&lt;0.0001</td>
<td>-0.338</td>
</tr>
<tr>
<td>Body nonfat weight (kg)</td>
<td>-0.378</td>
<td>&lt;0.0001</td>
<td>0.319</td>
<td>0.002</td>
<td>0.377</td>
</tr>
<tr>
<td>CD3+CD4+ count (cells/μl)</td>
<td>0.161</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virus load (IU/ml)</td>
<td>0.306</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up duration</td>
<td>0.192</td>
<td>&lt;0.0001</td>
<td>0.281</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NAFLD, nonalcoholic fatty liver disease. TG, triglyceride. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. UA, uric acid.

Table 3. Multiple stepwise regression analysis of influencing factors, including age, anthropometric parameters, immunological and virological indicators on lipid and uric metabolism parameters (n=61)
<table>
<thead>
<tr>
<th>Independent variable</th>
<th>B</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>constant</td>
<td>3.224</td>
<td>0.681</td>
<td>-</td>
<td>4.733</td>
<td>0.000</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>0.053</td>
<td>0.017</td>
<td>0.781</td>
<td>3.161</td>
<td>0.002</td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>0.031</td>
<td>0.007</td>
<td>0.369</td>
<td>4.249</td>
<td>0.000</td>
</tr>
<tr>
<td>Body nonfat weight (kg)</td>
<td>-0.064</td>
<td>0.028</td>
<td>-0.578</td>
<td>-2.319</td>
<td>0.023</td>
</tr>
<tr>
<td>Follow-up weeks</td>
<td>0.006</td>
<td>0.002</td>
<td>0.269</td>
<td>3.308</td>
<td>0.000</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>constant</td>
<td>18.767</td>
<td>5.130</td>
<td>-</td>
<td>3.658</td>
<td>0.001</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>0.902</td>
<td>0.192</td>
<td>3.564</td>
<td>4.696</td>
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</tr>
<tr>
<td>Body nonfat weight (kg)</td>
<td>-0.768</td>
<td>0.157</td>
<td>-1.883</td>
<td>-4.889</td>
<td>0.000</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>-1.684</td>
<td>0.477</td>
<td>-1.798</td>
<td>-3.528</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>0.095</td>
<td>0.042</td>
<td>0.293</td>
<td>2.249</td>
<td>0.031</td>
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<tr>
<td>HDL-c (mmol/L)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>constant</td>
<td>1.153</td>
<td>0.169</td>
<td>-</td>
<td>6.805</td>
<td>0.000</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.070</td>
<td>0.015</td>
<td>0.791</td>
<td>4.699</td>
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</tr>
<tr>
<td>CD3+CD4+ count (cells/ul)</td>
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<td>0.000</td>
<td>0.423</td>
<td>4.930</td>
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</tr>
<tr>
<td>Body weight (kg)</td>
<td>-0.028</td>
<td>0.004</td>
<td>-1.145</td>
<td>-6.174</td>
<td>0.000</td>
</tr>
<tr>
<td>LDL-c (mmol/L)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>constant</td>
<td>1.056</td>
<td>0.374</td>
<td>-</td>
<td>2.827</td>
<td>0.006</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.073</td>
<td>0.017</td>
<td>0.396</td>
<td>4.222</td>
<td>0.000</td>
</tr>
<tr>
<td>Follow-up weeks</td>
<td>0.003</td>
<td>0.002</td>
<td>0.173</td>
<td>1.847</td>
<td>0.068</td>
</tr>
<tr>
<td>UA (μmol/L)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>constant</td>
<td>323.772</td>
<td>15.315</td>
<td>-</td>
<td>21.141</td>
<td>0.000</td>
</tr>
<tr>
<td>Virus load (IU/ml)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.313</td>
<td>2.032</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Abbreviations: TG, triglyceride. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. UA, uric acid.

Figures

**Figure 1**
Effectiveness of ART with TDF plus 3TC plus EFV primary treatment for human immunodeficiency virus-infected male patients (n=61). A. CD4+ T cell count. B. viral load. C. The percentage of viral load reaching undetectable levels. Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV. Efavirenz. One-way ANOVA was used to compare CD4+ T cell count, viral load and the percentage of viral load reaching undetectable levels between different time points. ****P<0.0001.

Figure 2

Long-term dynamic changes in anthropometric parameters over 144 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61). A. body weight. B. body nonfat weight. C. body mass index. D. body fat weight. E. body fat percentage. Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. ANOVA was used to compare anthropometric parameters from baseline to 144 weeks, and a paired t-test was used to compare anthropometric parameters between baseline and some follow-up time points. Comparison between different time points and compared with baseline, *P<0.05, ** P<0.01, ***P<0.001, ****P<0.0001.
Figure 3

Long-term dynamic changes in lipid metabolic parameters over 144 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61). A. TC level. B. LDL-c level. C. HDL-c level. D. TG level. Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. TG, triglyceride. ANOVA was used to compare lipid metabolism parameters from baseline to 144 weeks, and a paired t-test was used to compare lipid metabolism parameters between baseline and some follow-up time points. Comparison between different time points and compared with baseline, *P<0.05, ** P<0.01, ***P<0.001, ****P<0.0001.
Figure 4

Long-term dynamic changes in the percentage of dyslipidemia over 144 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61). A. The percentage of hypercholesterolemia (TC>5.18 mmol/L). B. The percentage of hyper low-density lipoprotein cholesterolemia (LDL-c>3.37 mmol/L). C. The percentage of hypo high-density lipoprotein cholesterolemia (HDL-c<1.00 mmol/L). D. The percentage of hypertriglyceridemia (TG>1.7 mmol/L). Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. TG, triglyceride. The Kruskal-Wallis H(K) test for K independent samples was used to compare the percentage of dyslipidemia from baseline to 144 weeks. The Mann-Whitney test for two independent samples was used to compare the percentage of dyslipidemia between baseline and follow-up time points. Comparison between different time points and compared with baseline, *P<0.05, **P<0.01, ***P<0.001.
Long-term dynamic changes in UA and the percentage of hyperuricemia (UA > 420 μmol/L) over 144 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61). A. UA level. B. the percentage of hyperuricemia. Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. UA, uric acid. ANOVA was used to compare UA levels from baseline to 144 weeks, and a paired t-test was used to compare UA levels between baseline and some follow-up time points. The Kruskal-Wallis H(K) test for K independent samples was used to compare the percentage of hyperuricemia from baseline to 144 weeks. The Mann-Whitney test for two independent samples was used to compare the percentage of hyperuricemia between baseline and follow-up time points. Comparison between different time points and compared with baseline, all P>0.05.
Figure 6

Long-term effect of baseline CD4+ T cell count on lipid metabolism parameters within 96 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61; 26, 12, 23 cases in the <200, 200 to 350, and >350 groups, respectively). A. TC level. B. LDL-c level. C. HDL-c level. D. TG level. Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. TC, total cholesterol. LDL-c, low-density lipoprotein cholesterol. HDL-c, high-density lipoprotein cholesterol. TG, triglyceride. One-way ANOVA was used to compare lipid metabolism parameters between three groups at the same time point, and Two-way ANOVA was used to compare lipid metabolism parameters between three groups from baseline to 96 weeks. Comparison between different time points and different CD4+ T cell count groups, *P<0.05, **P<0.01, ****P<0.0001.
Figure 7

Long-term effect of baseline CD4+ T cell count on UA level within 96 weeks after initial highly active antiretroviral therapy with TDF plus 3TC plus EFV in treatment-naive patients with HIV (n=61, 26, 12, 23 cases in <200, from 200 to 350, >350 groups, respectively). Abbreviations: TDF, Tenofovir. 3TC, Lamivudine. EFV, Efavirenz. UA, uric acid. One-way ANOVA was used to compare UA between three groups at the same time point, and Two-way ANOVA was used to compare UA between three groups from baseline to 96 weeks. Comparison between different time points and different CD4+ T cell count groups, all P>0.05.