The CD4 slope can be a predictor of immunologic recovery in advanced HIV patients: a case-control study

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INTRODUCTION

Although the number of newly diagnosed human immunodeficiency virus (HIV) infections each year is reducing, there were still 35.0 million people were living with HIV and 1.5 million who died of HIV-related infections in 2013 [1]. The key clinical features of untreated HIV patients are, impaired immune function and increased risk of disease progression and death [2,3]. Since zidovudine (ZDV) was first introduced as an antiretroviral therapy in 1987, treatment has greatly improved due to the advent of ...
tent combination therapies in 1996 [3,4]. Combination therapies, known as highly active antiretroviral therapy (HAART), have been significantly effective in reducing and maintaining HIV loads at below detectable levels [2]. Despite the aviremic status achieved by HAART, HIV infection cannot be eradicated because of the persistence of the HIV in CD4 T cells [5,6]. Therefore, the primary goals of HAART are not only to suppress the plasma HIV load, but also to restore immunologic function, reduce opportunistic infections (OIs), and improve the survival of infected patients [3].

On receiving HAART, immunologic responses in patients are assessed by means of increases in their CD4 T cell counts. The immunologic response under HAART is a three-phase process. In the first phase, during 2 to 3 months after HAART initiation, the number of peripheral CD4 T cells increases rapidly, at an average rate of 20 to 30 cells/mm$^3$/month [2,7-9]. This is due to the redistribution of memory CD4 T cells from the lymphoid tissue to the blood compartment. The second phase lasts until the end of the second year of HAART, during which CD4 T cells increase by 5 to 10 cells/mm$^3$/month. Thereafter, in the third phase, the incremental pace of CD4 T cell count slows to 2 to 5 cells/mm$^3$/month [8,10]. During the latter two phases, mostly naïve CD4 T cells increase by various mechanisms: de novo production of T cells in the thymus, homeostatic proliferation of residual CD4 T cells, and the extension of the half-life of CD4 T cells [2,11].

Despite successful virologic suppression, however, some patients fail to achieve an adequate immunologic response. Old age and coinfection with other viruses, such as hepatitis C virus (HCV), are among the factors associated with a poor immunologic response. A baseline CD4 T cell count < 200/mm$^3$ when starting HAART is also a risk factor of poor immunologic response [2,9-16]. Nevertheless, some advanced patients with baseline CD4 T cell counts < 200/mm$^3$ do achieve adequate immunologic recovery [15]. The predictive factors of immunologic recovery in advanced HIV-infected patients were investigated in this study.

**METHODS**

**Study population**

Adult HIV-infected patients who visited a university-affiliated hospital in 1991 to 2011 and had received HAART for ≥ 4 years were enrolled in the study. The HAART regimen was defined as a combination of three antiretroviral drugs, including a combination of two nucleoside reverse-transcriptase inhibitors (NRTIs) and one of following: either a non-NRTI, a protease inhibitor (PI), or an integrase strand transfer inhibitor [3]. The HAART regimen was classified as NNRTI-based, boosted PI-based, unboosted PI-based, and mixed, according to the backbone of antiretroviral drugs administered. A boosted PI-based regimen was defined as a ritonavir-boosted PI-containing regimen. A mixed regimen was defined as a switch from one class to another [3].

Laboratory data were collected every 2 to 6 months to monitor patients after initiation of HAART. Because the objective of this study was to identify predictive factors of immunologic recovery in virologically suppressed patients, the analysis was restricted to those patients who achieved and maintained virologic suppression for ≥ 4 years with adequate medication adherence. Virologic suppression was defined as plasma HIV-1 RNA loads of < 50 copies/mL. Virologic failure was defined as two consecutive HIV-1 RNA loads > 200 copies/mL [3,17]. Intermittent viremia, defined as HIV-1 RNA loads being mostly < 50 copies/mL but only temporarily rising over 50 copies/mL, was not regarded as a virologic failure. To eliminate the effects of previous treatments, these patients were included only if the end of a previous treatment regimen had occurred at least 1 year from the start of the current treatment.

Immunologic responders (case group) were defined as patients showing CD4 T cell counts ≥ 500/mm$^3$ at 4 years after HAART initiation, and immunologic non-responders (control group) were those who did not [10,18]. The two groups were compared for various clinical and laboratory parameters, including the “CD4 slope,” to assess factors associated with immunologic recovery. Medical records were reviewed, including age, sex, route of HIV transmission, time interval between HIV diagnosis and HAART initiation, comorbidities, HAART regimen, OIs, and clinical stage at the start of HAART. Clinical categories of HIV infection were classified ac-
cording to the 1993 revised classification system of the Centers for Disease Control and Prevention (CDC), and OIs were defined as the clinical conditions listed in the surveillance case definitions for HIV infection and acquired immunodeficiency syndrome (AIDS) in the CDC [10]. Coinfections of hepatitis B virus (HBV) and of HCV were defined as being positive for HBV surface antigen, anti-HCV antibody, and HCV polymerase chain reaction, respectively.

The CD4 T cell count was measured using a Cytomics FC 500 (Beckman Coulter, Brea, CA, USA), and plasma HIV-1 RNA loads were measured by COBAS AmpliPrep/COBAS TaqMan HIV-1 Test (Roche Molecular Diagnostics, Pleasanton, CA, USA).

**Statistical analysis**

Univariate analysis of continuous variables was performed by t, Mann-Whitney U, or median tests, as appropriate. Categorical variables were compared between the case and control groups by a chi-square test. Multivariate analysis was performed using logistic regression. The CD4 slope, representing the CD4 T cell count change per month (cells/mm$^3$/month), was calculated for each patient as the slope of a best-fit line obtained by linear regression of CD4 T cell counts during a certain treatment period, against the time since HAART initiation: If there were three CD4 T cell results during 0- to 12-month period; for example, (0 month, 100 cells/mm$^3$; 4 months, 300 cells/mm$^3$; and 10 months, 500 cells/mm$^3$), a linear regression analysis was performed with these 3 data points. The best-fit line was calculated, and its slope was designated as the CD4 slope during 0 to 12 months.

All statistical analyses were performed using IBM SPSS version 20 (IBM Co., Armonk, NY, USA). A two-sided $p < 0.05$ was considered to indicate statistical significance.

**Ethics statement**

This study was approved by the Institutional Review Board of the Pusan National University Hospital (Protocol No. E-2013012) according to the Declaration of Helsinki. The requirement for informed consent was waived by the board.

**RESULTS**

A total of 102 patients met the inclusion criteria. Their mean age was 44.9 years, and 85.3% were male. The baseline CD4 T cell count (mean ± SD) was 129.9 ± 109.5/mm$^3$. Fifty-nine (57.8%) were immunologic responders, and 43 (42.2%) were non-responders (Table 1). Baseline CD4 T cell counts (mean ± SD) were 173.4 ± 113.1/mm$^3$ and 70.1 ± 69.6/mm$^3$ in responders and non-responders, respectively ($p < 0.001$). OIs at the start of HAART were more frequent in non-responders than in responders (51.2% vs. 33.9%), but this was not statistically significant ($p = 0.080$). The most frequent OI was tuberculosis (TB) (8/58 in responders and 9/43 in non-responders). There were no differences between responders and non-responders in age, time from diagnosis of HIV infection to initiation of HAART, CDC HIV-1 categories, and HBV or HCV coinfection.

To exclude the influences of baseline CD4 T cell counts, factors associated with immunologic recovery were analyzed in 73 advanced patients with baseline CD4 cell counts < 200/mm$^3$ (Table 2). Thirty-three patients (45.2%) were responders. Baseline CD4 T cell counts were 89.7 ± 57.8 and 57.1 ± 51.3/mm$^3$ in responders and non-responders, respectively ($p = 0.013$). OIs at the start of HAART were more frequent in non-responders than in responders (50.5% vs. 27.3%, $p = 0.048$).

**CD4 slope**

We calculated the CD4 slopes during 0 to 6 and 0 to 12 months of HAART. Due to the large number of missing CD4 slope data during 6 to 12 months, CD4 slope during 6 to 12 months was not analyzed. For all 102 patients, the CD4 slopes during 0 to 6 and 0 to 12 months of HAART, respectively, were significantly higher in responders than in non-responders (Fig. 1): the medians for responders and non-responders were 36.8 cells/mm$^3$/month vs. 21.3 cells/mm$^3$/month (0 to 6 months, $p = 0.024$) and 20.9 cells/mm$^3$/month vs. 13.5 cells/mm$^3$/month (0 to 12 months, $p = 0.001$). This was also the case for the 73 advanced patients with baseline CD4 T cell counts < 200/mm$^3$ (Fig. 2): the medians for responders and non-responders were 38.6 cells/mm$^3$/month vs. 22.8 cells/mm$^3$/month (0 to 6 months, $p = 0.005$) and 24.5 cells/mm$^3$/month vs. 13.5 cells/mm$^3$/month (0 to 12 months, $p < 0.001$).
Table 1. Clinical and laboratory characteristics of all 102 patients according to their immunologic responses to highly active antiretroviral therapy

| Characteristic                              | Responder (n = 59) | Non-responder (n = 43) | p value |
|---------------------------------------------|--------------------|------------------------|---------|
| Age, yr                                     | 44.9 ± 9.3         | 44.8 ± 10.8            | 0.969   |
| Male sex                                    | 49 (81.1)          | 38 (88.4)              | 0.454   |
| Route of HIV transmission                   |                    |                        | 0.328   |
| Heterosexual contact                        | 34 (57.6)          | 28 (65.1)              |         |
| Male homosexual contact                     | 25 (42.4)          | 14 (32.6)              |         |
| Transfusion                                 | 0                  | 1 (2.3)                |         |
| Time from diagnosis of HIV infection to initiation of HAART, day | 572.5 ± 895.2 | 746.6 ± 1,312.8 | 0.418   |
| Baseline CD4 T cell/mm³                     | 173.4 ± 113.1      | 70.1 ± 69.6            | < 0.001 |
| Baseline CD4 T cell count < 200/mm³         | 33 (55.9)          | 40 (93.0)              | < 0.001 |
| Baseline CD4 T cell count < 50/mm³          | 10 (16.9)          | 23 (53.5)              | < 0.001 |
| Baseline viral load > 100,000 copies/mL³    | 49 (83.1)          | 35 (81.4)              | 0.829   |
| CDC HIV-1 disease category b                |                    |                        | 0.357   |
| A                                           | 30 (50.8)          | 15 (34.9)              |         |
| B                                           | 11 (18.6)          | 7 (16.3)               |         |
| C                                           | 18 (30.5)          | 21 (48.8)              |         |
| Hepatitis B or C coinfection                | 6 (10.2)           | 5 (11.6)               | 0.815   |
| Syphilis                                    | 30 (50.8)          | 22 (51.2)              | 0.975   |
| Opportunistic infections at the start of HAART c | 20 (33.9) | 22 (51.2)              | 0.680   |
| Tuberculosis                                | 8 (13.6)           | 9 (20.9)               | 0.324   |
| Pneumocystis pneumonia                      | 7 (11.9)           | 8 (18.6)               | 0.343   |
| Cytomegalovirus disease                     | 2 (3.4)            | 2 (4.7)                | 0.746   |
| Cryptococcal meningitis                     | 0                  | 3 (7.0)                | 0.639   |
| Esophageal candidiasis                      | 1 (1.7)            | 2 (4.7)                | 0.383   |
| Treatment-naïve when starting HAART         | 57 (96.6)          | 42 (97.7)              | 0.753   |
| HAART regimen d                             |                    |                        | 0.443   |
| Unboosted PI-based                          | 20 (33.9)          | 13 (30.2)              |         |
| Boosted PI-based                            | 17 (28.8)          | 18 (41.9)              |         |
| NNRTI-based                                 | 16 (27.1)          | 7 (16.3)               |         |
| Mixed                                       | 6 (10.2)           | 5 (11.6)               |         |
| HAART regimen including ZDV                 | 51 (86.4)          | 39 (90.7)              | 0.510   |
| TMP/SMX use                                 | 29 (49.2)          | 32 (74.4)              | 0.010   |
| Duration of TMP/SMX use, mon                |                    |                        | 0.001   |
| < 1                                         | 31 (52.5)          | 14 (32.6)              |         |
| 1–6                                         | 15 (25.4)          | 6 (14.0)               |         |
| 7–12                                        | 10 (16.9)          | 6 (14.0)               |         |
| ≥ 13                                        | 3 (5.1)            | 17 (39.5)              |         |

Values are presented as mean ± SD or number (%).

HIV, human immunodeficiency virus; HAART, highly active antiretroviral therapy; CDC, Centers for Disease Control and Prevention; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; ZDV, zidovudine; TMP/SMX, trimethoprim/sulfamethoxazole.

aThere was one missing value in the responders and two in the non-responders.

bAccording to the CDC classification [19].

cDefined as the surveillance case definitions for HIV infection and acquired immunodeficiency syndrome (AIDS) of CDC [19].

dAccording to the backbone antiretroviral drugs. The boosted PI-based regimen is defined as a ritonavir boosted PI-containing regimen. The mixed regimen is defined as switching from one class to another [19].
Table 2. Clinical and laboratory characteristics of the 73 advanced patients according to their immunologic responses to highly active antiretroviral therapy

| Characteristic                              | Responder (n = 33) | Non-responder (n = 40) | p value |
|---------------------------------------------|-------------------|------------------------|---------|
| Age, yr                                     | 44.0 ± 7.3        | 44.7 ± 11.1            | 0.754   |
| Male sex                                    | 27 (81.8)         | 35 (87.5)              | 0.530   |
| Route of HIV transmission                   |                   |                        | 0.328   |
| Heterosexual contact                        | 17 (51.5)         | 26 (65.0)              |         |
| Male homosexual contact                     | 16 (48.5)         | 13 (32.5)              |         |
| Transfusion                                 | 0                 | 1 (2.5)                |         |
| Time from HIV diagnosis to HAART, day       | 545.4 ± 1,017.6   | 737.8 ± 1,346.8        | 0.490   |
| Baseline CD4 T cell/mm³                     | 89.7 ± 57.8       | 57.1 ± 51.3            | 0.013   |
| Baseline CD4 T cell count < 50/mm³          | 10 (30.3)         | 23 (57.5)              | 0.114   |
| Baseline viral load > 100,000 copies/mL     | 31 (93.9)         | 33 (82.5)              | 0.171   |
| CDC HIV-1 disease category<sup>a</sup>      | 13 (39.4)         | 12 (30.0)              | 0.647   |
| A                                           | 13 (39.4)         | 12 (30.0)              |         |
| B                                           | 4 (12.1)          | 7 (17.5)               |         |
| C                                           | 16 (48.5)         | 21 (52.5)              |         |
| Hepatitis B or C coinfection                | 2 (6.1)           | 5 (12.5)               | 0.446   |
| Syphilis                                    | 16 (48.5)         | 18 (45.0)              | 0.766   |
| Opportunistic infections at the start of HAART<sup>b</sup> | 9 (27.3) | 20 (50.0) | 0.048 |
| Tuberculosis                                | 7 (21.2)          | 9 (22.5)               | 0.895   |
| Pneumocystis pneumonia                      | 7 (21.2)          | 8 (20.0)               | 0.898   |
| Cytomegalovirus disease                     | 2 (6.1)           | 2 (5.0)                | 1.000   |
| Cryptococcal meningitis                     | 0                 | 3 (7.5)                | 0.247   |
| Esophageal candidiasis                      | 0                 | 2 (5.1)                | 0.498   |
| Treatment-naïve when starting HAART         | 32 (97.0)         | 39 (97.5)              | 1.000   |
| HAART regimen<sup>c</sup>                   |                   |                        | 0.677   |
| Unboosted PI-based                          | 11 (33.3)         | 12 (30.0)              |         |
| Boosted PI-based                            | 10 (30.3)         | 16 (40.0)              |         |
| NNRTI-based                                 | 9 (27.3)          | 7 (17.5)               |         |
| Mixed                                       | 3 (9.1)           | 5 (12.5)               |         |
| HAART regimen including ZDV                 | 28 (84.8)         | 36 (90.0)              | 0.723   |
| TMP/SMX use                                 | 27 (81.8)         | 31 (77.5)              | 0.650   |
| Duration of TMP/SMX use, mon                |                   |                        | 0.002   |
| < 1                                         | 7 (21.2)          | 12 (30.0)              |         |
| 1–6                                         | 13 (39.4)         | 5 (12.5)               |         |
| 7–12                                        | 10 (30.3)         | 6 (15.0)               |         |
| ≥ 13                                        | 3 (9.1)           | 17 (42.5)              |         |

Values are presented as mean ± SD or number (%).

HIV, human immunodeficiency virus; HAART, highly active antiretroviral therapy; CDC, Centers for Disease Control and Prevention; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitors; ZDV, zidovudine; TMP/SMX, trimethoprim/sulfamethoxazole.

<sup>a</sup>According to the CDC classification [19].

<sup>b</sup>Defined as the surveillance case definitions for HIV infection and acquired immunodeficiency syndrome (AIDS) of CDC [19].

<sup>c</sup>According to the backbone antiretroviral drugs administered. The boosted PI-based regimen is defined as a ritonavir boosted PI-containing regimen. The mixed regimen is defined as switching from one class to another [19].
The CD4 slope during 0 to 12 months of HAART was also analyzed as a dichotomous categorical variable with a cutoff of 20 cells/mm$^3$/month. For all 102 patients, the proportion of those with a CD4 slope during 0 to 12 months $\geq$ 20 cells/mm$^3$/month was significantly higher in responders (2 missing values; 30/57, 52.6%) than in non-responders (7/43, 16.3%), and the unadjusted odds ratio (OR) was 5.71 (95% confidence interval [CI], 3.32 to 32.61). Likewise, for the 73 advanced patients with baseline CD4 T cell counts < 200/mm$^3$, the proportion was also significantly higher in responders (21/33, 63.6%) than in non-responders (7/40, 17.5%) with an unadjusted OR of 8.25 (95% CI, 2.80 to 24.31).

Multivariate analyses to identify independent predictors for immunologic recovery after HAART
Univariate analyses of all 102 patients showed that 20 of 59 responders (33.9%) and 22 of 43 non-responders (51.2%) had OIs when starting HAART, but this difference was not statistically significant (unadjusted OR, 0.49; 95% CI, 0.22 to 1.10). Multivariate analyses, however, showed that OIs at the start of HAART were independently associated with poor immunologic response (adjusted OR, 0.28; 95% CI, 0.10 to 0.83) (Table 3).

Baseline CD4 T cell counts $\geq$ 200/mm$^3$ (adjusted OR, 19.83; 95% CI, 3.73 to 105.48) and a CD4 slope $\geq$ 20 cells/mm$^3$/month during 0 to 12 months (adjusted OR, 10.41; 95% CI, 3.32 to 32.61) were also independently associated with immunologic recovery (Table 3). Multivariate analysis of the 73 advanced HIV-infected patients with baseline CD4 T cell counts < 200/mm$^3$, identified that independent predictors for immunologic recovery were an absence of OIs and a CD4 slope $\geq$ 20 cells/mm$^3$/month during 0 to 12 months, but not a baseline CD4 T cell count $\geq$ 100/mm$^3$ (Table 3).

DISCUSSION
HAART successfully suppressed HIV-1 replication and reduced HIV-associated morbidity and mortality [3]. However, in some patients, immunologic response after HAART was not adequate, despite their aviremic status. There is no definite consensus on the definition of non-responders, but generally, they are defined as patients with CD4 T cell counts $< 500$ cells/mm$^3$ after 4 to 7 years of treatment, because CD4 T cell count of 500 cells/mm$^3$ represents the lower limit of the physiological range [10,18]. In previous studies, 20% to 49.7% of patients receiving HAART did not achieve immunolog-
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This study showed that 42.2% (43/102) of patients were non-responders.

Our results also showed that trimethoprim/sulfamethoxazole (TMP/SMX) use was significantly less frequent in responders, but it was not an independent predictor for poor immunologic recovery in multivariate analysis (Table 3). Because TMP/SMX is primarily used for the prevention of Pneumocystis jirovecii pneumonia in patients with CD4 T cell counts < 200/mm$^3$ and is taken until CD4 T cell counts reach and maintain > 200/mm$^3$ [21], its use is more a consequence of poor immunologic recovery than a cause.

ZDV was previously a preferred and widely used choice for NRTI backbone, but ZDV is no longer recommended due to side effects including gastrointestinal intolerance, fatigue, and anemia [3]. In addition, ZDV may have a toxic effect to hematopoietic cells and could interrupt immunologic recovery [2]. In our results, most patients received ZDV-containing regimen, so there were no differences between responders and non-responders (Tables 1 and 2).

In the Australian HIV Observational Database, not having any prior AIDS-defined illness was a predictor of the time taken to achieve CD4 T cell counts > 500 cells/mm$^3$ [16]. In this study, for all patients, OIs were more frequent in non-responders than in responders, but this was not statistically significant. However, in multivariate logistic regression analysis, OIs at the start of HAART were an independent predictive factor for immunologic recovery (adjusted OR, 0.28; 95% CI, 0.10 to 0.83; $p = 0.022$) (Table 3).

TB is an OI in HIV-infected patients, and it is known that treatment of TB before starting HAART, can lead to a slight increase in CD4 T cell counts [19,22]. In this study, few patients had TB (Tables 1 and 2) and the CD4 slope during 0 to 12 months of HAART was not significantly different between responders with TB and those without (data not shown, $p = 0.658$). Because HAART was initiated after a 2-month period of intensive TB treatment for these patients, it is conceivable that neither TB nor its treatment influenced the CD4 slope during the first year of HAART.

During the first phase of HAART, memory CD4 T cells sequestered within lymphoid tissues were redistributed into the peripheral blood. In the second and third phases, naïve CD4 T cells increased via production in the thymus [9,15,23,24]. Because thymic output is impaired in older patients, this represents a higher risk for reduced CD4 recovery than in younger patients [2,25]. In this study, however, age was not a predictive factor of immunologic recovery (Tables 1 and 2). This may be because the majority of patients were aged < 50 years. There were no differences in the CD4 slopes after 12 months of HAART (later phases) between responders and non-responders (Figs. 1 and 2), probably due to the similar age distribution in both groups.

In this study, we analyzed the CD4 slope during 0 to 12 months of HAART as a dichotomous categorical variable with a cutoff of 20 cells/mm$^3$/month. In a previous study, failure to achieve a CD4 count increase > 100 cells/mm$^3$ in 12 months on HAART is defined as immunologic failure [26]. However, because the objective of this study was to identify immunologic recovery in patients with virological suppression, we set the cutoff of CD4 slope during 0 to 12 months higher than in previous reports.

Within a group of similarly aged patients, the redistribution of memory CD4 T cells during the first phase

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Table 3. Multivariate logistic regression analysis to identify independent predictors of immunologic recovery

| Parameter                                      | All 102 patients | 73 Advanced patients |
|-----------------------------------------------|-----------------|----------------------|
|                                               | Adjusted OR (95% CI) | p value | Adjusted OR (95% CI) | p value |
| TMP/SMX use                                   | 0.99 (0.28–3.51) | 0.985     | NA                  | NA      |
| Opportunistic infections at the start of HAART | 0.28 (0.10–0.83) | 0.022     | 0.28 (0.08–0.94)    | 0.039   |
| Baseline CD4 T cell count ≥ 200 cells/mm$^3$  | 19.81 (3.73–105.48) | < 0.001 | NA                  | NA      |
| Baseline CD4 T cell count ≥ 100 cells/mm$^3$  | NA               | NA       | 2.61 (0.81–8.40)    | 0.107   |
| CD4 slope ≥ 20/mm$^3$/mon during 0–12         | 10.41 (3.32–32.61) | < 0.001 | 10.10 (3.06–33.30)  | < 0.001 |

OR, odds ratio; CI, confidence interval; TMP/SMX, trimethoprim/sulfamethoxazole; NA, not applicable; HAART, highly active antiretroviral therapy.
would therefore be related to immunologic recovery, and the initial CD4 slope during the earlier phase of HAART could possibly be a predictor for this recovery. In this study, the CD4 slopes during 0 to 6 and 0 to 12 months were significantly higher in responders than in non-responders (Table 3, Figs. 1 and 2). These findings correspond with those in a previous study (the Swiss HIV Cohort Study), showing significant differences between the CD4 slopes of responders and non-responders [20].

Lower baseline CD4 T cell counts are associated with poor immunologic response [20,27]. In this study, the baseline CD4 T cell count was also a predictive factor for CD4 recovery in all 102 patients, but not in the 73 advanced patients with baseline CD4 T cell counts < 200/mm³. On the other hand, a CD4 slope ≥ 20/mm³/month at 0 to 12 months after HAART was a predictive factor for CD4 recovery in all patients, including the advanced HIV patients. Therefore, in patients with advanced HIV disease, a CD4 slope ≥ 20 cells/mm³/month during 0 to 12 months can be a better predictor for CD4 T cell recovery than a baseline CD4 T cell count. This result can be a useful indicator in countries where early diagnosis of HIV infection is not well-established due to limited resources, and where patients presenting with advanced HIV disease are common.

In conclusion, the CD4 slope can be calculated by linear regression with two or more CD4 T cell counts, enabling its use as a predictive factor for long-term immunologic recovery.

KEY MESSAGE

1. Opportunistic infections at the start of highly active antiretroviral therapy (HAART) and a CD4 slope ≥ 20 during 0 to 12 months of HAART were independently associated with immunologic recovery.
2. The CD4 slope can be a predictor of immunologic recovery in advanced human immunodeficiency virus patients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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