HIV/AIDS - Research and Palliative Care
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ORIGINAL RESEARCH

DLCO in HIV Patients and Their Association with CD4 and VL

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Introduction: The advent of highly active antiretroviral therapy (HAART) has changed infection by human immunodeficiency virus (HIV) from an acute disease to a manageable chronic condition; however, pulmonary complications continue to affect patient quality of life. The goal of this research was to examine the link between CD4+ levels, viral load, and respiratory function in patients infected with HIV.

Methods: Patients were grouped as HIV-infected and non-infected (1:2 ratio). The analysis included between-group comparisons of the post-bronchodilator FEV1, FVC, FEV1/FVC ratio, forced expiratory flows at various lung volumes (FEF75, FEF50, FEF75/25), and carbon monoxide diffusion capacity (DLCO). We analyzed CD4+ counts and viral load effects on lung function using stepwise regression. For normally distributed continuous variables (presented as means ± SD), intergroup comparisons were performed using independent two-sample *t*-tests. Non-normal distributions (reported as medians [IQR]) were analyzed with Mann–Whitney *U*-tests. Categorical variables were compared using χ^2 or Fisher's exact tests, with statistical significance set at $p < 0.05$.

Results: The study enrolled 150 participants infected with HIV with a mean age of 48 (39.25, 57.75) years; 87.33% were male and 46% had a history of smoking. The DLCO was significantly lower in patients with HIV (69.37 vs 82.23, $p < 0.05$) compared to patients without HIV. In patients with HIV, the DLCO was positively correlated with CD4+ T lymphocyte counts ($r=0.5521$, $p < 0.0001$) and negatively correlated with the HIV viral load ($r=-0.3942$, $p < 0.0001$), and both were statistically significant. Patients with CD4+ ≥ 200 cells/μL had significantly higher VC (89.52 vs 79.31), FVC (91.80 vs 83.55), FEV1 (91.60 vs 84.40), and DLCO (74.61 vs 57.96) than those with CD4+ < 200 cells/μL. Similarly, patients with undetectable viral loads had higher VC (87.99 vs 81.08), FVC (90.90 vs 83.70), and DLCO (72.59 vs 60.62) than those with detectable viremia (all $p < 0.05$). The CD4+ count and FVC were significant predictors of the DLCO ($p < 0.05$).

Conclusion: HIV infection is significantly associated with impaired pulmonary diffusion function. Even after antiviral therapy when the viral load becomes undetectable (CD4+ T lymphocytes > 400), the impairment of pulmonary diffusion still persists. Therefore, we should strengthen the pulmonary function testing for AIDS patients, detect the risk of lung injury as early as possible, carry out timely interventions, and reduce the risk of chronic obstructive pulmonary disease (COPD).

Keywords: HIV infection, lung function, DLCO, CD4+ cell, pulmonary complications

Introduction

The introduction of highly active antiretroviral therapy (HAART) has shifted Human Immunodeficiency Virus (HIV) from a life-threatening acute illness to a controllable chronic disease.[1] However, people living with HIV (PLWH) continue to face complex health challenges, and pulmonary complications are becoming a major concern.[2,3] The HIV-related pulmonary complications include airflow obstruction, impaired gas exchange, emphysema, Chronic Obstructive Pulmonary Disease (COPD), and interstitial lung disease.[4–6]

Received: 10 April 2025
Accepted: 9 August 2025
Published: 2 September 2025

Studies to date have primarily examined the effect of HIV infection on ventilatory function.[7–9] In 2018, Triplette et al found that markers of COPD were associated with increased mortality of PLWH.[10] In 2021, Rasmussen et al demonstrated that, even with virological suppression, individuals positive for HIV showed significantly greater annual declines in Forced Expiratory Volume in 1 second (FEV1), and forced vital capacity (FVC) than individuals negative for HIV, independent of smoking status.[7] Despite ART improving airflow obstruction, many virally suppressed patients with HIV still show abnormal diffusing capacity of the lungs for carbon monoxide (DLCO). This phenomenon is attracting increasing attention from researchers worldwide. Studies have linked DLCO decline to viral load,[11] but data on Asian populations remain limited. As of 2023, China's HIV-positive population exceeds 1.3 million, with annual new diagnoses consistently surpassing 100,000.[12] Currently, there is a lack of large-scale national statistics on COPD among people living with HIV (PLWH) in China. As of October 31, 2023, a total of 40,840 HIV-infected individuals and patients have been cumulatively reported in Beijing.[13] However, there are no reports or statistics on pulmonary function impairment in HIV patients in the Beijing area. Therefore, our study is deemed to be of significant necessity.

The present study aimed to compare the decline in DLCO between patients infected with HIV and controls who were not infected with HIV, and to examine its association with CD4+ cell counts and viral load, thereby providing insights for early intervention.

Patients and Methods

Study Population

This is a retrospective cross-sectional study. We analyzed patients who received pulmonary function testing at Beijing Ditan Hospital, Capital Medical University (a national-level infectious disease center with over 800 hospital beds in Beijing, China) between January 2019 and December 2024. A total of 4,299 individuals have completed pulmonary function tests (PFTs). The 4,299 study subjects were divided into HIV-positive and HIV-negative groups. One group comprised 150 patients infected with HIV, and the other group comprised 4149 individuals who were not infected with HIV. Infection with HIV and the AIDS diagnoses followed the Chinese Guidelines for the Diagnosis and Treatment of HIV/AIDS (2021 Edition).[14] All patient data (including demographic information, pulmonary function test results, CD4+T cell counts, and viral loads, etc) were extracted through the hospital's electronic medical record (EMR) system. The extraction process strictly adhered to the authority management regulations of the hospital's Information Department, with only core members of the authorized research team having access to the original data. Immediately after extraction, the data were anonymized by removing personally identifiable information such as names, ID card numbers, and medical record numbers, retaining only non-identifying variables necessary for the study (eg, age, gender, and test values).The research followed the principles of the Declaration of Helsinki and the study protocol received ethical approval from the Institutional Review Board of Beijing Ditan Hospital, Capital Medical University (Ethics Approval Number: DTEC-KY2024-012-01). Written informed consent was obtained from all participants prior to enrollment.

Methods

① We collected information from all patients with available pulmonary function test results, including 150 HIV-positive patients. These HIV-positive patients were matched with non-HIV patients at a ratio of 1:2 based on age, height, sex, and weight. For all participants infected with HIV, we simultaneously collected CD4+ T-cell counts and HIV viral loads. Pulmonary function testing was performed using an MSDIFFUSION APS system (Jaeger Company, Germany) to assess the FVC, FEV1, FEV1/FVC ratio, PEF, FEF75, FEF50, FEF25, and TLC. The carbon monoxide diffusion capacity (DLCO) was measured using the breathing method. All subjects completed pulmonary function tests (PFTs) adhering strictly to the American Thoracic Society/European Respiratory Society (ATS/ERS) protocol standards.[15] These tests involved spirometry both before and after the administration of bronchodilators, along with a single-breath DLCO test. Airflow obstruction was characterized as a post-bronchodilator FEV1/FVC ratio below 0.70.

Statistical Analysis

SPSS 26.0 statistical software was used for the data analytics. For normally distributed continuous variables (presented as means ± SD), intergroup comparisons were performed using independent two-sample *t*-tests. Non-normal distributions (reported as medians [IQR]) were analyzed with Mann–Whitney *U*-tests. Categorical variables were compared using χ^2 or Fisher's exact tests, with statistical significance set at $p < 0.05$.

Results

Demographic and General Characteristics

The cohort infected with HIV had a median age of 48 years (range: 19 to 85 years), 69 of whom were smokers. The median height was 170 cm, the median weight was 65 kg, and the average body mass index (BMI) was 22.5 kg/m². The majority of the patients were male, accounting for 87.33% of the total. The median $CD4^+$ was 289 cells/μL, the median $CD4^+$ /$CD8^+$ ratio was 0.47, and the median viral load was 0 (Table 1).

Patient Pulmonary Function Characteristics

Since pulmonary function results are affected by age, height, weight, and sex, and there were statistically significant differences between the two groups in these aspects (as shown in Table 2), HIV-positive patients were matched with HIV-negative controls at a 1:2 ratio in this study. After matching, no statistically significant differences were observed between the groups in these variables (all $p > 0.05$), as presented in Table 3. Pulmonary ventilation functions include atmospheric and small-airway ventilation and were primarily assessed using DLCO. Patients positive for HIV demonstrated a significantly higher FEV1/FVC ratio compared to the controls negative for HIV ($p < 0.05$), but the results were > 70% (81.94 vs 79.09). The actual-to-predicted FVC values in both groups were > 80%, and the results showed no significant differences (all p-values > 0.05) In terms of small airway ventilation function, statistically significant differences were observed between the patients infected with HIV versus the patients not infected with HIV in MMEF75/25 (71.90 vs 66.30), FEF 50 (79.10 vs 71.50), and FEF75 (92.50 vs 83.20) ($p < 0.05$). However, all values remained above 65%, suggesting no small airway obstruction. In terms of lung ventilation, the DLCO was significantly lower in

Table 1 Demographics and General Characteristics of HIV Patients

Variable	**HIV Patients (N=150)**
Age	48.00 (39.25, 57.75)
Smoking history	69 (46.0%)
Height	170.00 (165.00, 175.00)
Weight (kg)	65.00 (58.25, 75.00)
Sex, n (%)	
Male	131 (87.33)
Female	19 (12.67)
CD4+ cells (μ/l)	289 (82, 530)
$CD4^+$cells/ $CD8^+$cells	0.47 (0.13,0.85)
VL	0 (0, 79,475)

Abbreviations: CD4+ cells, CD4 - positive T - lymphocytes; CD4+ cells/CD8+ cells, CD4 - positive T - lymphocytes/CD8 - positive T – lymphocytes; VL, Viral Load.

Table 2 Demographics of HIV Patients and Non-HIV Patients

Variable	Total (n = 4299)	HIV-negative (n = 4149)	HIV-postive (n = 150)	*P*
Age	53.00 (35.00, 65.00)	53.00 (35.00, 65.00)	48.00 (39.25, 57.75)	0.051
Height	167.00 (160.00, 172.00)	167.00 (160.00, 172.00)	170.00 (165.00, 175.00)	<0.001
Weight	67.00 (59.00, 75.00)	67.00 (59.00, 76.00)	65.00 (58.25, 75.00)	<0.001
Sex, n (%)				<0.001
Male	2356 (54.8)	2225 (53.63)	131 (87.33)	
Female	1943 (45.2)	1924 (46.37)	19 (12.67)	

Table 3 Demographics and General Characteristics of HIV Patients and Non-HIV Patients

Variable	Total (n = 435)	0 (n = 290)	1 (n = 145)	*P*
Age	51.00 (35.00, 63.00)	52.00 (33.00, 64.00)	49.00 (40.00, 58.00)	0.513
Height	170.00 (165.00, 175.00)	170.00 (165.00, 175.00)	170.00 (165.00, 175.00)	0.483
Weight	65.00 (58.00, 74.00)	65.00 (57.00, 72.88)	66.00 (60.00, 75.00)	0.318
Sex, n (%)				0.807
Male	374 (85.98)	248 (85.52)	126 (86.90)	
Female	61 (14.02)	42 (14.48)	19 (13.10)	

Table 4 Comparison of Pulmonary Function Between HIV Patients and Non-HIV Patients

	Total (n=435)	HIV-negative (n=290)	HIV-positive (n=145)	P value
FVC	89.70 (76.35,102.55)	91.30 (77.00,103.30)	88.00 (74.95,100.53)	0.073
FEV1	89.20 (73.80,100.15)	89.50 (73.50,101.10)	88.50 (74.15,97.03)	0.562
FEV1/FVC	80.05 (73.62,102.55)	79.09 (72.33,84.01)	81.94 (76.85,87.35))	0.000
FEF50	74.90 (49.00,94.55)	71.50 (45.65,91.75)	79.10 (58.70,103.90)	0.000
FEF75	85.00 (60.45,103.48)	83.20 (57.80,101.30)	92.50 (64.40,110.10)	0.007
MMEF75/25	69.20 (45.90,88.15)	66.30 (43.00,86.70)	71.90 (53.42,95.23)	0.020
DLCO	78.13±20.90	82.23±19.26	69.37±21.63	0.000

Abbreviations: FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume in 1 second; FEV1/FVC, Ratio of Forced Expiratory Volume in 1 second to Forced Vital Capacity; FEF50, Forced Expiratory flow at 50% of Forced Vital Capacity; FEF75, Forced Expiratory Flow at 75% of Forced Vital Capacity; MMEF75/25, Maximal Mid-expiratory Flow between 75% and 25% of Forced Vital Capacity; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide.

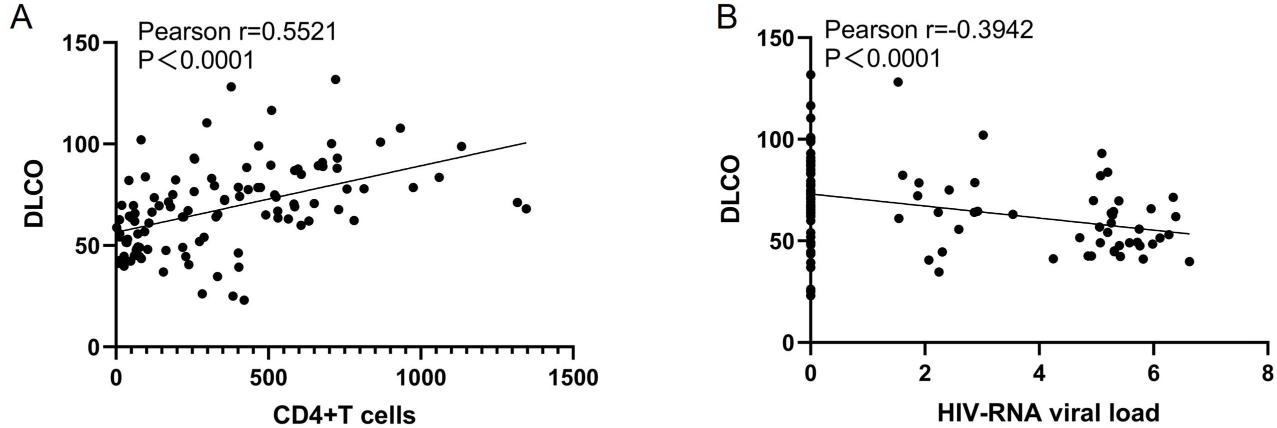

Figure 1 (**A**) Diffusing capacity of the lung for carbon monoxide (DLCO) is positively correlated with CD4+ T cells. (**B**) DLCO is negatively correlated with the HIV viral load.

the patients infected with HIV compared to the patients not infected with HIV-infected (69.37 vs 82.23, $p < 0.05$), indicating impaired lung diffusion function in the group with HIV. Further details are presented in Table 4.

Correlation Analysis Among DLCO, $CD4^+$ T-Cell Counts, and Viral Loads

We conducted linear correlation analyses to assess the relationships between the DLCO and both CD4+ T-cell counts and HIV viral loads. Statistical analysis revealed a strong positive association between DLCO and CD4+ levels (Pearson's r=0.5521, $p < 0.0001$), as shown in Figure 1A. However, the DLCO was negatively correlated with the HIV viral load (r= −0.3942), and the correlation was statistically significant ($p < 0.0001$), as shown in Figure 1B.

Among the patients with HIV, there were 119 patients with $CD4^+$T cell count records, 73 patients with $CD4^+$T lymphocytes ≥ 200 cells/μL, and 46 patients with $CD4^+$T lymphocytes < 200 cells/μL, all of who were mainly male, accounting for 84%. For the patients with $CD4^+$T lymphocytes ≥ 200, the VC (89.52 vs 79.31), FVC (91.80 vs 83.55), FEV1 (91.60 vs 84.40), and DLCO (74.61 vs 57.96) were significantly higher than those in the group with $CD4^+$T lymphocytes < 200. The results were statistically significant ($p < 0.05$), as shown in Table 5. Among the patients with HIV, 117 patients had records of their viral load results, 68 patients had undetected viral loads, 49 patients had detectable viral loads, and they were mainly male, accounting for 86.3%. The VC (87.99 vs 81.08), FVC (90.90 vs

Table 5 Comparison of the Pulmonary Function of Patients with a CD4 Count Greater Than 200 and Those with a CD4 Count Less Than 200 Cells/μL

	Total (n=119)	**$CD4^+$ ≥200 (n=73)**	**$CD4^+$<200 (n=46)**	**P value**
Male	100 (84%)	59 (80.8%)	41 (89.1%)	0.000
VC	85.57±18.04	89.52±17.33	79.31±17.54	0.002
FVC	88.20 (75.80, 99.40)	91.80 (81.15,102.25)	83.55 (67.25,91.98)	0.003
FEV1	89.00 (76.40, 97.20)	91.60 (81.35, 100.95)	84.40 (69.88,92.88)	0.011
FEV1/FVC	81.99 (77.09, 87.76)	81.56 (76.05,85.28)	84.57 (77.70,89.40)	0.141
DLCO	67.95±21.04	74.61±22.23	57.96±14.31	0.000

Abbreviations: $CD4^+$, CD4-positive T lymphocyte; VC, Vital Capacity; FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume in 1 second; FEV1/FVC, Ratio of Forced Expiratory Volume in 1 second to Forced Vital Capacity; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide.

https://doi.org/10.2147/HIV.S532629

Table 6 Comparison of the Pulmonary Function of Patients with VL>20 Copies and Those with Undetectable VL

	Total (n=117)	VL <20 (n=68)	VL≥20 (n=49)	P value
Male	101 (86.3%)	56 (82.4%)	45 (91.8%)	0.000
VC	85.09±17.92	87.99±18.52	81.08±16.41	0.039
FVC	86.80 (74.15, 99.35)	90.90 (78.68, 101.70)	83.70 (68.25, 94.75)	0.039
FEV1	88.80 (75.35, 96.85)	90.80 (80.63, 100.13)	85.80 (72.40, 93.25)	0.099
FEV1/FVC	82.44 (77.31, 87.85)	81.21 (75.25, 84.90)	86.01 (79.80, 90.03)	0.002
DLCO	67.27±20.64	72.59±21.13	60.62±18.10	0.002

Abbreviations: VL, Viral Load; VC, Vital Capacity; FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume in 1 second; FEV1/FVC, Ratio of Forced Expiratory Volume in 1 second to Forced Vital Capacity; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide.

83.70), and DLCO (72.59 vs 60.62) of the patients in the group with undetected viral loads were significantly higher than those in the group with detectable viral loads ($p < 0.05$), as shown in Table 6.

With the advent of the HIV antiviral era, an increasing number of patients have achieved undetectable viral loads. We evaluated the DLCO levels in these patients. As shown in the Table 7 below, 65 patients had undetectable viral loads and an average DLCO of 69.69%, which was below the normal value. The average $CD4^+$ cell count was 476 cells/μL.

To establish the key determinants of DLCO, we performed a stepwise regression analysis. Stepwise regression analysis identified the $CD4^+$ count and FVC as significant predictors of the DLCO ($p < 0.05$), as shown in Figure 2 below. The model had an R^2 of 0.497 and the adjusted R^2 was 0.487, indicating that the $CD4^+$ count and FVC explained approximately 48.7–49 of the variation in the DLCO. The standard error of the estimate was 15.011, indicating a high predictive accuracy and strong correlation of the DLCO with the $CD4^+$ count and FVC.

Discussion

In this study, we found that lung ventilation function in patients infected with HIV was significantly reduced, as evidenced by a significant decrease in the DLCO (69.37 vs 82.23), which was positively correlated with the $CD4^+$ cell count and negatively correlated with viral load, both with statistical significance. We divided the patients with HIV into two groups, with a $CD4^+$ T lymphocyte count of 200 as the threshold value. We found that the DLCO was significantly reduced in the patients with $CD4^+$ T cell count < 200 cells/μL (57.96 vs 74.61), and the difference was statistically significant. We divided the patients with HIV into two groups based on whether they had a detectable viral load. We found that in patients with detectable viral replication, the DLCO also decreased significantly (60.62 vs 72.59),

Table 7 The Level of DLCO in HIV Patients with Viral Load Below the Detection Limit

	HIV Patients (n=65)
$CD4^+$ cells	476±260
$CD4^+$ cells/$CD8^+$ cells	0.74 (0.48, 1.08)
DLCO	69.69±21.28

Abbreviations: $CD4^+$ cells, CD4-positive T lymphocyte; CD4+ cells/CD8+ cells, CD4 - positive T - lymphocytes/ CD8 - positive T – lymphocytes; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide.

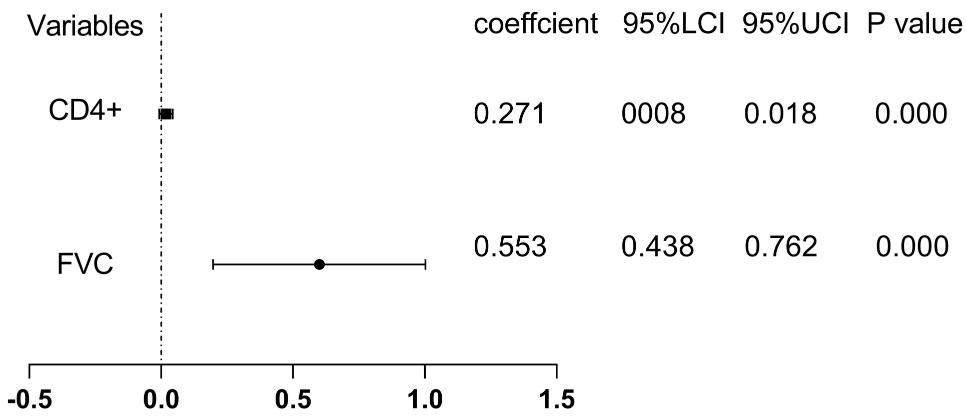

Figure 2 CD4+ and FVC are important factors influencing the diffusing capacity of the lung for carbon monoxide (DLCO).

and the difference was statistically significant. Stepwise regression analysis revealed that the $CD4^+$ cell count and FVC were important factors affecting the DLCO ($p < 0.05$).

Smoking is a known risk factor for pulmonary function impairment, which can directly damage lung structures by inducing COPD, small airway inflammation, and pulmonary diffusion dysfunction. In this study, the smoking rate among HIV-infected individuals (46%) was significantly higher than that in the general population, suggesting that this population may face a dual risk of lung injury from "HIV infection + smoking".

We observed a significant decrease in the DLCO, with an average of 67.95%, regardless of the $CD4^+$ and viral load levels in patients with HIV. Recently, concern has grown regarding the impairment of lung carbon monoxide diffusion capacity observed in patients with AIDS.[16,17] A recent meta-analysis on the impact of HIV on lung function showed that a decrease in the DLCO is the most common pulmonary impairment in patients infected with HIV, with prevalence rates ranging from 6–30%[18–20] and 39–75% for DLCO < 60% and DLCO < 80%, respectively,[19–23] independent of obstructive pulmonary disease and emphysema. This reduction is associated with increased symptoms, worsening health, and increased mortality. Studies have also shown that impaired lung diffusion capacity is associated with all-cause mortality in individuals infected with HIV during a mean follow-up period of 6 years,[24] suggesting that DLCO is an independent clinically important marker. However, all of these data are from Europe and the United States, and there are no relevant data for Asians. Our study shows that the average DLCO of patients with HIV and CD4 < 200 (36.7%) was 57.96% (< 60%), and the average DLCO of patients with HIV and CD4 ≥ 200 (61.3%) was 74.61% (< 80%). Our results are consistent with those of the meta-analysis and fill the gaps in data on Asians. Islain et al study found that in patients infected with HIV and CD4+ < 200 µL/mL, the mean DLCO was 56.31%, and in patients with a detectable viral load, the mean DLCO was 59.46%.[11] In our study, for patients with CD4 < 200 µL/mL, the mean DLCO was 57.96%, and for patients with detectable disease load, the mean DLCO was 60.62%, which is consistent with the findings of Islain et al. This indicates that the degree of impairment of pulmonary diffusion function caused by HIV is comparable between Asian and other ethnic groups. Our study provides additional supporting evidence and fills the gap in data for Asian populations. Previous studies have focused primarily on the impact of viral load on lung function. However, our stepwise regression analysis found that the CD4+ count and FVC are significant factors affecting the DLCO, with little correlation with viral load. This suggests that immune function recovery is a key determinant of lung function status.

CD4- T lymphocytes play a central role in immune function.[25] HIV primarily targets CD4- T lymphocytes, leading to a progressive decline in the count and subsequent immune system impairment. When the $CD4^+$ T lymphocyte count decreases to below a certain threshold, patients are prone to various opportunistic infections and lung injuries such as pneumocystis pneumonia and cytomegalovirus pneumonia.[26] These lung lesions can lead to damage to the alveolar-capillary membranes as well as pulmonary interstitial fibrosis, resulting in a decrease in the DLCO. This correlation suggests that the DLCO may be used as an additional indicator to reflect the overall state of the immune system in patients with HIV and assist in evaluating disease progression. In contrast, the HIV viral load reflects the replication level of HIV in the body. The higher the viral load, the more active the replication of HIV is in the body, triggering more intense immune activation and inflammatory responses.[27] This persistent inflammatory state can lead to inflammatory cell infiltration into the lung tissue and alveolar structure destruction, thereby affecting gas exchange and reducing the DLCO.[28] A high viral load may also directly invade lung tissue cells such as alveolar epithelial cells and vascular endothelial cells, resulting in cell damage, dysfunction, and destruction of lung diffusion function.[18] Additionally, a high viral load promotes pulmonary fibrosis, further impairing lung diffusion capacity. This association suggests that DLCO monitoring may serve as a useful tool to evaluate immune recovery and antiretroviral therapy efficacy. This association provides a new way of thinking about clinical treatment; namely, monitoring the DLCO may help with the evaluation of patient immune recovery and the effectiveness of antiviral therapy. As the patient's immune status recovers, the DLCO should theoretically improve, providing a potential, noninvasive, complementary means of evaluating treatment effectiveness.

Nevertheless, several limitations should be considered for this study. First, the sample size was limited to cases in the Beijing area, which may not fully represent the diversity of broader populations infected with HIV. Second, while the correlation was evident, the underlying molecular mechanisms remain unexplored. Future studies should expand the sample size to include patients infected with HIV from diverse regions, disease courses, and treatment stages to further validate and refine this correlation. Additionally, molecular biology techniques should be employed to elucidate the signaling pathways linking the viral load, immune status, and lung function to enhance the understanding of HIV-induced pulmonary impairment.

Conclusions

In summary, the results of PFTs in this study reveal a key phenomenon: even when HIV-infected patients receive adequate antiviral therapy and achieve a clinically controlled state with undetectable viral load and CD4+T lymphocyte count > 400, their DLCO remains persistently impaired. This finding not only confirms that the potential long-term impact of HIV infection on the lungs does not entirely depend on the activity of viral replication but also suggests that there may be a "desynchrony" between the apparent recovery of immune function (such as the increase in CD4+T cell count) and the pathophysiological repair of lung parenchyma. This dissociated state provides a new perspective for understanding the chronic mechanism of HIV-related pulmonary complications.

From the perspective of clinical practice, this result emphasizes that the necessity of monitoring pulmonary function in HIV patients should not be limited to the achievement of virological or immunological indicators. Clinicians need to incorporate early and regular pulmonary function assessments (especially DLCO testing) into long-term management plans. By dynamically tracking changes in pulmonary diffusing function, subclinical lung injuries can be accurately identified, providing a basis for timely interventions (such as targeted respiratory rehabilitation or anti-inflammatory therapy) and thereby delaying the progression of irreversible impairment of pulmonary function.

Ethics

The study protocol received ethical approval from the Institutional Review Board of Beijing Ditan Hospital, Capital Medical University (Ethics Approval Number: DTEC-KY2024-012-01).

Acknowledgments

No funding was received for this study.

Disclosure

The authors declare that they have no competing interests in this work.

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