

Prevalence and risk factors for bone mineral density changes in antiretroviral therapy-naive human immunodeficiency virus-infected adults: a Chinese cohort study

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Abstract

Background Studies have reported that low bone mineral density (BMD) is prevalent in human immunodeficiency virus (HIV)-infected patients; however, the factors that contribute to HIV-related BMD changes are yet to be fully understood. Due to the application of dual X-ray absorptiometry (DXA) among a select group of hospitals only, the prevalence and risk factors of low BMD in HIV-infected populations have not been intensively investigated in China. Thus, the aim of our study was to investigate the prevalence of and risk factors associated with BMD changes among antiretroviral therapy (ART)-naive HIV-positive patients in China.

Methods The assessment of the prevalence of and risk factors associated with BMD changes was conducted among 156 ART-naive HIV-infected patients. Demographic and clinical data, as well as results of fasting blood tests were obtained from patients. Further, all patients underwent DXA scans to determine BMD, which was then used to classify patients with osteopenia/osteoporosis. The risk factors of reduced BMD were then evaluated using binary logistic regression.

Results Among the 156 ART-naive HIV-infected participants, osteopenia and osteoporosis were diagnosed in 48.7% (76/156) and 4.5% (7/156) of patients, respectively. The lumbar spine was most likely to have reduced BMD (49.4% [77/156]), and the proportion of osteopenia in the left hip (32.7% [51/156]) was higher than in the right hip (24.4% [38/156]). In the lumbar spine, bone loss rate in the L1 section (60.9% [95/156]) was the most significant (L2, 53.2% [83/156]; L3, 45.5% [71/156]; L4, 52.6% [82/156]). Further analysis showed that, compared with the neck (26.9% [42/156] in the left, 18.6% [29/156] in the right) and the interior (15.4% [24/156] in the left, 13.5% [21/156] in the right), the trochanter had the greatest probability of reduced BMD (46.2% [72/156] in the left, 28.8% [45/156] in the right). In the risk factor analysis, low body mass index (BMI: <18.5 kg/m²) was positively associated with reduced BMD (Exp (B) = 39.743, 95% confidence interval: 3.234–488.399, *P* = 0.004), and was specifically positively correlated with BMD values at three sites (*r* = 0.335 at right hip, *r* = 0.327 at left hip, *r* = 0.311 at lumbar spine).

Conclusion Reduced BMD was found in the majority of ART-naive HIV-infected patients and BMI was identified as an additional risk factor for reduced BMD. Our results show that BMD reduction was simultaneously present in the left hip, right hip, and lumbar spine among nearly one fifth of patients. Our work highlights the importance of closely monitoring BMD in ART-naive patients and provides a foundation for the clinical intervention of bone demineralization in them.

Keywords: Human immunodeficiency virus (HIV); Antiretroviral therapy-naive; Bone mineral density; Body mass index

Introduction

According to the joint assessment of the Chinese Center for Disease Control and Prevention and the World Health Organization (WHO), by the end of 2018, 1.25 million people were living with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) in China.^[1] In the past 3 years, the number of newly discovered infections has reached 13 thousand per year,

and as such, the health status of HIV-infected patients has received widespread attention. Due to the advent of antiretroviral therapy (ART), the life expectancy of HIV-infected individuals has gradually increased,^[2-5] but premature aging and AIDS-related diseases, including osteopenia and bone fractures, have gradually gained prominence. Currently, there are sufficient data demonstrating a higher prevalence of bone fractures among HIV-infected patients than among non-HIV-infected patients,

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thus indicating an association between the two.^[6-8] A previous meta-analysis suggested that the risk of bone fracture in HIV-infected patients was 1.35 fold higher than that of HIV-uninfected controls.^[9] The China AIDS Treatment Guidelines (2018 Edition),^[10] recommend that HIV-infected patients in China should initiate ART; however, tenofovir (TDF)-based antiretroviral regimens could reduce bone mineral density (BMD), resulting in osteopenia and even fracture. Moreover, the rising average age of the HIV-infected population, the long-term repercussions of an uncontrolled HIV infection, and extended exposure to ART may further contribute to BMD loss, resulting in heavier medical burdens and higher costs for public health systems. It is, therefore, necessary to identify risk factors and high-risk sites of HIV-related osteopenia and fractures to help physicians provide clinical interventions for these patients. In recent years, international studies have found some underlying factors and mechanisms that contribute to osteopenia and bone fractures in HIV-infected patients,^[11-15] including the pro-inflammatory effects of chronic HIV infection, aging, endocrine dysfunction (such as menopause), low calcium and vitamin D intake, smoking, and body mass index (BMI).

Although some studies outside of China have evaluated the prevalence and risk factors of osteopenia,^[16-18] there are no prior studies addressing these issues in ART-naive HIV-infected patients in China. In this study, we retrospectively analyzed the prevalence, location, and risk factors of osteopenia in Chinese ART-naive HIV-infected patients. Our aim is to assist physicians in diagnosing and providing clinical intervention and thus reduce or alleviate the occurrence of HIV-related bone diseases and improve patients' quality of life.

Methods and materials

Ethical approval

Our study protocol was conducted in accordance with the *Declaration of Helsinki* and approved by the Ethics Committees of Beijing Ditan Hospital (No. 2019-045-001). All eligible patients gave written informed consent for this study.

Population and study design

HIV-infected patients were recruited between July 2018 and December 2018 from the Clinical and Research Center of Infectious Diseases, Beijing Ditan Hospital, Capital Medical University. Inclusion criteria were: patient who (1) has not initiated ART; (2) is Chinese; (3) does not have hyperthyroidism, hyperparathyroidism, hypogonadism, diabetes mellitus, menopause, opportunistic infection and does not use corticosteroids, or have previous calcium and vitamin D supplementation.

We first collected demographic information and grouped patients by age (<40 years; ≥40 years), smoking status (smoker, non-smoker), drinking status (current drinker, non-current drinker), and exercising status (exerciser, non-exerciser) in order to assess whether such parameters were risk factors for reduced BMD.

The BMI of patients was then calculated by dividing weight by the squared height (kg/m^2). Patients were categorized according to the Overweight/Obese Medicine Nutrition Therapy Expert Consensus in China (2016 edition): underweight (BMI <18.5 kg/m^2), normal weight (BMI of 18.5–23.9 kg/m^2), overweight (BMI of 24.0–27.9 kg/m^2), or obese (BMI ≥28.0 kg/m^2).^[19]

Concurrently, laboratory examinations were conducted, including routine blood tests, liver function tests (bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate transaminase, γ -glutamyl transferase, and albumin), renal function tests (including urea and creatinine), bone profile (blood calcium, phosphate), lipid profile, fasting plasma glucose, syphilis status, hepatitis B and C serology, CD4⁺ T cell counts, and HIV-1 RNA levels.

Finally, participants enrolled in this study received dual X-ray absorptiometry (DXA) scans at the lumbar spine (L1–L4), and the right and left hips (femur neck, trochanter, and interior), using a HOLOGIC X-ray absorptiometry scanner (HOLOGIC Discovery A Bone, Boston, MA, USA). BMD was measured using DXA scans and recorded as g/cm^2 . A standardized protocol was used to obtain BMDs of the total hip and lumbar spine.^[20] T scores (male patients ≥50 years) or Z scores (male patients <50 years) of less than or equal to –1 were used to define a reduced BMD based on the WHO classification (osteoporosis: score ≤ –2.50 and osteopenia: score between –2.49 and –1.01).^[20]

Statistical analysis

First, we performed a descriptive statistical analysis. We used median (interquartile range) and mean ± standard deviation for non-normally and normally distributed data, respectively. Different statistical tests were used, as appropriate. Statistically significant differences between two independent groups were analyzed using the Student's *t* test and Wilcoxon rank-sum test for normally and non-normally distributed continuous data, respectively. Comparisons between more than two groups were performed using a one-way analysis of variance. Binary logistic regression models were used to identify risk factors for reduced BMD. Finally, significant correlations between two quantitative variables were analyzed using Spearman *r* correlation coefficient. A *P* value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics for IOS version 24 (IBM Corp, Armonk, NY, USA).

Results

A total of 156 patients were enrolled in this study, and DXA scans of the lumbar spine, left, and right hip were conducted. Among the 156 patients, 73 (46.8%) presented with normal BMD, while 76 (48.7%) and 7 (4.5%) were diagnosed as osteopenia and osteoporosis, respectively. The demographic and clinical characteristics of the two patient groups are detailed in Table 1.

All 156 study participants were male and ART-naive, with a median age of 28 (25, 32) years. Among them, 82.7%

Table 1: Baseline characteristics of ART-naive HIV-infected patients in the analysis.

Characteristics	Normal BMD group (n = 73)	Low BMD group (n = 83)	Statistics	P
Age (years)	29.0 (25.0, 32.5)	27.0 (24.0, 31.0)	2736*	0.296
Hepatitis C Ab positive	0	0	–	–
Hepatitis B sAg positive	4 (5.5)	5 (6.0)	–	1.000
Syphilis positive	15 (20.5)	14 (16.9)	0.348†	0.555
Current smoker	32 (43.8)	43 (51.8)	0.989†	0.320
Current drinker	25 (34.2)	31 (37.3)	0.162†	0.687
Current exerciser	37 (50.7)	42 (50.6)	0.000†	0.992
BMI (kg/m ²)	23.0 (21.2, 25.7)	21.1 (19.6, 23.0)	1932*	<0.001
Education			0.149†	0.928
Third level	40 (54.8)	43 (51.8)		
Secondary level	21 (28.8)	25 (30.1)		
Primary level	12 (16.4)	15 (18.1)		
Any history of fracture	9 (12.3)	13 (15.7)	0.356†	0.551
HIV transmission risk group			4.782†	0.092
Homosexual	57 (78.1)	72 (86.8)		
Heterosexual	8 (11.0)	2 (2.4)		
Other	8 (11.0)	9 (10.8)		
HIV RNA			0.926†	0.629
Low VL level (VL <1000 copies/mL)	13 (17.8)	19 (22.9)		
Median VL level (1000 ≤ VL <100,000 copies/mL)	51 (69.9)	52 (62.7)		
High VL level (VL ≥100,000 copies/mL)	9 (12.3)	12 (14.5)		
CD4 ⁺ T cell (cells/mm ³)	330 ± 148	307 ± 143	0.970‡	0.333
CD8 ⁺ T cell (cells/mm ³)	821 (605, 1132)	987 (664, 1163)	3492*	0.100
CD4/CD8	0.36 (0.27, 0.52)	0.35 (0.20, 0.46)	2565*	0.099
Laboratory variables				
ALT (U/L)	22.10 (15.65, 35.05)	18.00 (12.50, 31.40)	2570*	0.103
AST (U/L)	20.30 (17.25, 28.95)	19.90 (16.80, 26.20)	2794*	0.403
Albumin (g/L)	48.00 (46.20, 49.50)	47.70 (45.50, 49.50)	2872*	0.577
TG (mmol/L)	2.30 (2.26, 2.36)	2.31 (2.26, 2.37)	2612*	0.139
CHO (mmol/L)	4.04 ± 0.76	3.88 ± 0.80	1.245‡	0.215
LDL-C (mmol/L)	2.43 (2.00, 2.77)	2.38 (1.81, 2.87)	2822*	0.461
HDL-C (mmol/L)	0.91 (0.79, 1.12)	0.96 (0.84, 1.10)	3158*	0.649
BUN (mmol/L)	4.75 (4.10, 5.72)	4.45 (3.80, 5.11)	2439*	0.036
Cr (μmol/L)	69.8 (64.4, 76.2)	69.4 (63.2, 77.3)	3025*	0.986
Blood calcium (mmol/L)	2.31 ± 0.09	2.31 ± 0.08	0.106‡	0.916
Phosphate (mmol/L)	0.99 (0.88, 1.09)	0.98 (0.88, 1.10)	3134*	0.712

Data are presented as mean ± standard deviation, median (Q₁, Q₃) or n (%). * U values. † χ² values. ‡ t values. Ab: Antibody; ALT: Alanine aminotransferase; ART: Antiretroviral therapy; AST: Aspartate transaminase; BMD: Bone mineral density; BMI: Body mass index; BUN: Blood urea nitrogen; CHO: Cholesterol; Cr: Creatinine; HDL-C: High density lipoprotein-cholesterol; HIV: Human immunodeficiency virus; LDL-C: Low density lipoprotein-cholesterol; sAg: Surface antigen; Secondary level: High school; Primary level: Junior high school and below; TG: Triglyceride; Third level: University and postgraduate qualifications; VL: Viral load.

(129/156) of patients were infected through homosexual contact, and the median CD4⁺ T cell count was 322 (220, 401) cells/mm³. Regarding clinical variables, median BMI was 21.9 (20.1, 24.7) kg/m², 48.1% (75/156) of patients were smokers, 35.9% (56/156) were current drinkers, 5.8% (9/156) had hepatitis B co-infection, and 18.6% (29/156) had syphilis co-infection.

Table 2 presents the results of lumbar spinal BMD (total, L1, L2, L3, L4), and left and right hip BMD (total, femur neck, trochanter, interior) of the 156 patients. Based on WHO definitions, 83 (53.2%) patients were diagnosed with reduced BMD (osteopenia or osteoporosis) in at least one site, 22 (14.1%) had reduced BMD in one site, 30 (19.2%) in two sites, and 31 (19.9%) in all three sites. Seven of the 83 patients with reduced BMD presented with T-scores or Z-scores of < -2.5 (all

in the lumbar spine) and were classified as having osteoporosis.

We found that the BMD Z/T scores of the lumbar spine, left hips, and right hips were significantly different from one another ($F = 30.115$, $P < 0.001$). The prevalence of osteopenia in the left hip, right hip, and lumbar spine was 32.7% (51 cases), 24.4% (38 cases), and 49.4% (77 cases), respectively [Table 2]. These results indicate that the lumbar region is the location most prone to develop osteopenia in ART-naive patients, followed by the left hip and finally the right hip, which had almost half the frequency of osteopenia in the lumbar region.

The difference among the lumbar vertebrae (L1–L4) was also significant ($F = 4.189$, $P = 0.006$). Osteopenia was most commonly developed in the L1 vertebra (95 cases,

Table 2: BMD Z/T scores of ART-naive HIV-infected patients in this study (n = 156).

Items	Patients with low BMD	Z/T-scores	Minimum Z/T scores	Maximum Z/T scores	F	P
Lumbar spine	77 (49.4)	-0.94 ± 0.95	-3.30	1.40	4.189	0.006
Site of the lumbar spine						
L1	95 (60.9)	-1.16 ± 0.95	-3.50	1.50		
L2	83 (53.2)	-0.94 ± 0.97	-3.40	1.50		
L3	71 (45.5)	-0.76 ± 1.00	-3.40	1.70		
L4	82 (52.6)	-0.90 ± 1.10	-3.70	1.60		
Total left hip	51 (32.7)	-0.40 ± 0.85	-2.40	1.70	28.228	<0.001
Site of the left hip						
Femur neck	42 (26.9)	-0.33 ± 0.96	-2.20	2.10		
Trochanter	72 (46.2)	-0.83 ± 0.77	-2.40	1.20		
Interior	24 (15.4)	-0.12 ± 0.85	-2.20	2.00		
Total right hip	38 (24.4)	-0.18 ± 0.83	-2.10	2.00	20.284	<0.001
Site of the right hip						
Femur neck	29 (18.6)	-0.17 ± 0.96	-2.30	2.60		
Trochanter	45 (28.8)	-0.53 ± 0.74	-2.20	1.50		
Interior	21 (13.5)	0.09 ± 0.88	-1.90	2.30		

Data are presented as mean ± standard deviation or n (%). Patients younger than 50 years use Z scores, and patients aged 50 years and above use T scores. BMD: Bone mineral density; ART: Antiretroviral therapy; HIV: Human immunodeficiency virus.

Table 3: Z/T scores of different BMI patient groups.

Groups	n	BMI (kg/m ²)	Low BMD	Right hip Z/T scores	Left hip Z/T scores	Lumbar spine Z/T scores
LG	11	17.8 (17.0, 18.0)	9 (81.8)	-0.87 ± 0.60	-1.08 ± 0.64	-1.64 ± 0.84
NG	100	21.2 (20.0, 22.3)	59 (59.0)	-0.24 ± 0.83	-0.47 ± 0.84	-1.01 ± 0.93
OAOG	45	26.1 (25.2, 27.9)	15 (33.3)	0.10 ± 0.76	-0.09 ± 0.82	-0.60 ± 0.93
All	156	21.9 (20.1, 24.7)	83 (53.2)	-0.18 ± 0.83	-0.40 ± 0.85	-0.94 ± 0.95

Data are presented as mean ± standard deviation, median (Q₁, Q₃) or n (%). BMI: Body mass index; BMD: Bone mineral density; LG: Lean group; NG: Normal group; OAOG: Overweight and obese group.

60.9%), while osteopenia was observed in the L2, L3, and L4 vertebrae in 83 cases (53.2%), 71 cases (45.5%), and 82 cases (52.6%), respectively [Table 2].

We further studied the site of osteopenia in the hip and found that the prevalence of osteopenia in the trochanter (46.2% [72/156] in the left, 28.8% [45/156] in the right) was significantly higher than that in the femoral neck (26.9% [42/156] in the left, 18.6% [29/156] in the right) and the interior (15.4% [24/156] in the left, 13.5% [21/156] in the right). Furthermore, the BMD Z/T scores in the trochanter, femur neck, and interior of both left and right hips were also significantly different ($F=28.228$, $P<0.001$ in the left, $F=20.284$, $P<0.001$ in the right), indicating that hip osteopenia is most prone to occur in the trochanter [Table 2].

Using Table 1, we determined that there was a significant difference in BMI between the normal and reduced BMD groups (23.0 [21.2, 25.7] vs. 21.1 [19.6, 23.0] kg/m², $U=1932$, $P<0.001$). In order to further understand the relationship between BMI and BMD, study participants were further divided into four groups: lean group (LG), normal group (NG), overweight group, and obese group according to their different BMI as categorized by China's Overweight/Obese Medicine Nutrition Therapy Expert Consensus (2016 edition). The overweight and obese groups were then combined into one group (OAOG) due

to the lack of statistical difference in Z/T score between the two groups. Further evaluation showed that the prevalence of reduced BMD was 81.8% (9/11) in the LG, 59.0% (59/100) in the NG, and 33.3% (15/45) in the OAOG group. Z/T scores of the right hip, left hip, and lumbar spine were significantly different among the three groups (right hip: $F=7.198$, $P=0.001$; left hip: $F=7.272$, $P=0.001$; lumbar spine: $F=6.547$, $P=0.020$), indicating that patients with lower BMIs were more prone to developing reduced BMD. Moreover, through Spearman correlation analysis, we found that BMI was significantly associated with bone loss at each of the three sites (left hip: $r=0.327$, $P<0.001$; right hip: $r=0.335$, $P<0.001$; lumbar spine: $r=0.311$, $P<0.001$) [Table 3].

Upon further study, the binary logistic regression model (backward selection method) also demonstrated that low BMI (BMI <18.5 kg/m², Exp (B) = 39.743, 95% confidence interval: 3.234–488.399, $P=0.004$) was a risk factor for osteopenia in ART-naive HIV-infected patients, while other factors, such as older age, CD4⁺ T cells, and viral load were not associated with reduced BMD [Table 4]. Interestingly, we found that there was a stronger correlation between the BMD of the left hip and the right hip ($r=0.933$, $P<0.001$) than that between the BMD of the hips and lumbar spine ($r=0.653$, $P<0.001$ between the left hip and lumbar spine; $r=0.639$, $P<0.001$ between the right hip and lumbar spine).

Table 4: Risk factors for low BMD in ART-naive HIV-infected patients by binary logistic regression analysis.

Characteristics	Exp (B)	95% CI	P
Age (years)			
<40	1		
≥40	2.302	0.613–8.646	0.217
Smoking status			
Never	1		
Usually	1.242	0.564–2.735	0.590
Drinking status			
Never	1		
Usually	1.138	0.525–2.468	0.743
Exercising status			
Never	1.806	0.849–3.842	0.125
Usually	1		
BMI (kg/m ²)			
<18.5	39.743	3.234–488.399	0.004
18.5–23.9	11.455	1.739–75.443	0.011
24.0–27.9	5.868	0.888–38.770	0.066
≥28.0	1		
HIV-related characteristics			
Baseline CD4 (cells/mm ³)			
CD4 <200	1.094	0.361–3.321	0.874
200 ≤ CD4 < 350	1.051	0.471–2.346	0.903
CD4 ≥350	1		
Baseline VL (copies/mL)			
VL <1000	1		
1000 ≤ VL < 100,000	0.937	0.388–2.265	0.885
VL ≥ 100,000	1.874	0.507–6.923	0.346
Laboratory results			
Syphilis status			
Negative	1		
Positive	0.654	0.268–1.595	0.350
Blood phosphate (mmol/L)	2.235	0.240–20.836	0.480
Blood calcium (mmol/L)	1.337	0.008–230.284	0.912
Albumin (g/L)	0.763	0.506–1.150	0.196
TG (mmol/L)	1.002	0.923–1.087	0.970
CHO (mmol/L)	0.991	0.556–1.767	0.975
LDL-C (mmol/L)	1.004	0.944–1.069	0.896
HDL-C (mmol/L)	0.777	0.190–3.167	0.724
ALT (U/L)	1.004	0.968–1.041	0.829
AST (U/L)	0.998	0.931–1.070	0.961

Results calculated by binary logistic regression (backward selection method). BMD: Bone mineral density; ART: Antiretroviral therapy; HIV: Human immunodeficiency virus; CI: confidence interval; BMI: Body mass index; VL: Viral load; TG: Triglyceride; CHO: Cholesterol; LDL-C: Low density lipoprotein-cholesterol; HDL-C: High density lipoprotein-cholesterol; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase.

Discussion

With the advent of ART, TDF-based antiretroviral regimens have been widely used in the HIV-infected population, which in turn has led to TDF-induced bone demineralization and a consequent gradual increase in the prevalence of osteopenia/osteoporosis. Many researchers have focused on the effect of antiretroviral drugs on BMD,^[21,22] but few studies have focused on bone demineralization among the ART-naive population. In our study, 156 ART-naive HIV-infected patients were recruited and underwent DXA scanning to screen for and diagnose HIV-related bone diseases. Our study indicated a high prevalence of reduced BMD among ART-naive HIV-infected patients. Some international studies have investigated the prevalence of osteoporosis and osteopenia in

HIV-infected cohorts and found that the prevalence ranged from 40% to 62%.^[23,24] In this study, 53.2% (83/156) of patients were diagnosed with reduced BMD (osteopenia or osteoporosis) based on DXA scans, which is consistent with previous studies.^[23,24]

In our study, we found that the lumbar spine was the most common site of bone demineralization and that bone demineralization occurred more frequently in the left hip than in the right hip. This is likely due to the dextrality in most people, which results in more exercised and stronger right sided limbs. In-depth analysis of the lumbar spine and the hips indicated that the L1 vertebrae had the highest prevalence of reduced BMD in the lumbar spine, while in the hip, reduced BMD was more likely to develop in the

trochanter. Bone demineralization was found in these sites (46.2% in the left trochanter, 28.8% in the right trochanter, and 60.9% in the L1 vertebrae) prior to patients fulfilling the clinical criteria for reduced BMD and with higher frequency than total left hip (32.7%), total right hip (24.4%), and total lumbar spine (49.4%). The distinct localization of osteopenia/osteoporosis to these anatomical sites, which has not been previously reported, provides clinicians with new specific targets for intervention in ART-naive patients. Since both the lumbar spine and hip are key anatomical sites of weight-bearing, initial recommendations would be to reduce weight-bearing activities in order to mitigate the burden on the skeleton system and avoid fragility fractures or other bone injuries.

We also found that BMI was a pivotal factor in BMD changes in ART-naive patients, while traditional risk factors, including age, smoking, and CD4 levels, were not associated with reduced BMD. International clinical trials for the assessment of bone disorders in HIV-infected populations have shown that reduced BMD was significantly associated with a lower BMI,^[25,26] and it has been reported that a higher BMI (>23.9 kg/m²) is a protective factor for reduced BMD among HIV-infected patients.^[25] In this study, we found that the BMD Z/T scores of overweight/obese patients were significantly higher than those with a normal BMI, which is consistent with the conclusion of previous studies.

The biological mechanisms driving HIV-related reduced BMD are diverse and could be due to a variety of sources such as long-term HIV infection, complicated chronic illness, malnutrition, malabsorption, and smoking and drinking. In this study, traditional risk factors, including age, smoking, and drinking, were not found to be associated with reduced BMD. This, however, could be due to one of the limitations of our study, which is the small sample size of study participants.

Our study has a few limitations. The study was carried out in a single center, and therefore conclusions derived from this work should be further validated in other centers in China. Additionally, because of the small sample size and the low heterogeneity of the enrolled patients, statistical power was low. Despite such limitations, our study provides unique insights. For example, this is the first study to investigate bone demineralization at the lumbar spine (L1–L4) as well as the three anatomic sites of the femur (trochanter, femoral neck, and interior) through DXA in ART-naive HIV-infected patients in China. Our findings highlight the importance of applying adequate strategies to prevent bone demineralization and provide the basis for monitoring and intervention in HIV-related BMD reduction.

We found that the prevalence of reduced BMD among ART-naive HIV-infected patients was 53.2%, and that lower BMI was a risk factor for reduced BMD. Additionally, our results suggest that reduced BMD simultaneously develops at the left hip, right hip, and lumbar spine among nearly one fifth of ART-naive patients. Both the lumbar spine and hip are key anatomical sites of weight-bearing, and thus it is necessary for patients to reduce weight-bearing exercises in order to mitigate the burden on the skeleton system. For the

first time, we determined that the L1 vertebrae in the lumbar spine and trochanter in the hips are particularly susceptible to BMD reduction, highlighting them as key targets for future monitoring. We also found that bone demineralization developed in these locations in ART-naive patients prior to fulfillment of clinical criteria for reduced BMD, which indicates them as predictive sites for physicians and possible clinical intervention sites for bone demineralization in ART-naive patients.

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Conflicts of interest

None.

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