Chronic kidney disease is related to femoral neck bone loss among HIV-1-infected patients : a retrospective study

Takashi MURAMATSU[1], Kagehiro AMANO[1,2], Yushi CHIKASAWA[1], Masato BINGO[1],

Mihoko YOTSUMOTO[1], Manabu OTAKI[1], Takeshi HAGIWARA[1],

Katsuyuki FUKUTAKE[1,2]

[1]Department of Laboratory Medicine, Tokyo Medical University
[2]Department of Molecular Genetics of Coagulation Disorders, Tokyo Medical University

Abstract

Reduced bone mineral density (BMD) is frequently observed in adults with HIV-1 infection. However, there is no sufficient information about the prevalence of BMD loss and its risk factors, including traditional and long-term comorbidities, in Japanese patients with HIV-1 infection. This was a single-center, retrospective study in Tokyo, Japan. HIV-1-infected patients over 40 years of age who visited our clinic between January 2013 and August 2014 were examined based on their medical chart and dual-energy X-ray absorptiometry (DXA) at the lumbar spine and femoral neck. Multivariate logistic regression was used to determine risk factors associated with low BMD, and linear regression was used to examine the relationship between low BMD and renal factors. Of the 306 patients (mean age, 49 years ; 96.4%, Japanese ; 95.1%, men ; median CD4 cell count, 520 cells/μL ; 96.1% on antiretroviral therapy) who met our criteria, 37.9% and 7.2% had osteopenia and osteoporosis, respectively, at the lumbar spine ; and 48.7% and 6.5%, respectively, at the femoral neck. Osteoporosis was revealed to have developed in their 40s. Multivariate analyses revealed an association between chronic kidney disease (CKD) and significantly lower BMD of the femoral neck (odds ratio, 1.999 ; 95% confidence interval, 1.078-3.812) as well as other risk factors (BMI, smoking, and years of exposure to ritonavir-boosted protease inhibitors). The DXA scan is necessary and feasible among Japanese HIV patients over 40 years of age. The present results demonstrated that CKD is an independent risk factor for femoral neck bone loss.

Introduction

There have been considerable improvements in survival among HIV-infected patients due to advances in antiretroviral therapy (ART). As HIV-infected patients live longer, age-related complications are becoming more prevalent among this population. In addition, HIV-infected patients tend to have more comorbidities than their non-HIV counterparts. Although HIV infection and opportunistic infection are manageable with adequate ART, long-term complications such as cardio-vascular disease (CVD), diabetes mellitus (DM), chronic kidney disease (CKD), and fractures are a growing concern among HIV patients[1]. Mortality in HIV-infected patients without risk factors on successful ART is almost identical to that in the non–HIV-infected population, and the prevention and treatment of complications are important for the long-term management of HIV-infected patients. Because osteoporosis is closely related to fragility fracture and a worse prognosis in patients with fracture among the general population[2], early intervention is essential in preventing such injuries. In one

study, for every one standard deviation decrease in BMD at the hip, there was a 2.6-fold increase in the risk of hip fracture[3]. Evaluation of BMD is considered the most reliable method to determine bone health and is a good predictor among elderly people.

Several HIV cohort studies have revealed a high prevalence of bone loss, osteoporosis[4], and bone fracture compared with the general population[5]. One meta-analysis showed that 67% of HIV-infected patients had osteopenia and 15% had osteoporosis[4]. HIV-related bone loss is due to three major causes : (1) the effect of HIV on bone, including HIV-induced chronic inflammation[6] ; (2) classical risk factors such as older age, smoking, low body weight, and excess alcohol (3 units/day)[7] ; and (3) the side effects of antiretroviral drugs (ARVs)[8]. Several recommendations regarding bone loss screening among HIV-infected patients have been proposed[9] ; however, uncertainty remains about the optimal timing of dual-energy X-ray absorptiometry (DXA) screening among HIV-infected patients.

Chronic kidney disease is the most important comorbidity among HIV-infected patients because of its high prevalence and predisposition to dialysis[10]. We investigated the prevalence of CKD among HIV-infected Japanese patients[11], and the results showed a higher prevalence than among the general population. It is also a risk factor for CVD, anemia, and bone disorders among the general population[12]. There are several reports that moderate to severe decreases in kidney function are associated with a 1.5- to 3-fold higher risk of fracture[13]. Chronic kidney disease-related bone fracture might become a major risk factor among the aged HIV population.

In this study, we retrospectively evaluated the result of DXA scanning of HIV-infected patients at our hospital and investigated the prevalence and risk factors for bone loss among HIV-infected patients. We analyzed the relation between BMD loss and HIV-related factors (including ARV exposure), CKD and other traditional risk factors.

Methods

Study design and participants

We performed a single-center, retrospective analysis in a hospital outpatient-based cohort and surveyed all patients attending for routine appointments between January 2013 and August 2014. We included patients who were 40 years old or older, and who had undergone a DXA scan at both the lumbar spine (L1-L4) and femoral neck in the study cohort ; the earliest scan in each patient was analyzed. Patient medical charts were screened for demographic data, age, race, sex, Body Mass Index (BMI) score, and blood and urinary test results, HIV-1 viral load, number of CD4+ cells, ART, ART regimen

with tenofovir disoproxil fumarate (TDF) and ART regimen with ritonavir-boosted protease inhibitor (PI/r). Patients were categorized as a current user or as a never/former user in terms of cigarette smoking and excessive alcohol consumption (greater than 3 units/day). Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or hypertension medication use. Diabetes mellitus was defined as a diagnosis of DM prior to baseline or the use of oral antidiabetic drugs or insulin at baseline. Dyslipidemia and CVD were defined as a diagnosis of either disease prior to baseline. Blood and urine data were obtained within 3 months before or after the date of the DXA scan. This study was conducted in accordance with "the Declaration of Helsinki" and the "Ethical Guidelines for Medical and Health Research Involving Human Subjects" (Public Notice of the Ministry of Health, Labour and Welfare of Japan, 2014). The Institutional Review Board, The Ethics Committee in Medical Research, reviewed and approved the study protocol on August 27, 2014 (No. 2820). Information on this research, including its purpose and the freedom to refuse to participate was made public between August 27, 2014 and October 30, 2014.

Bone mineral density

A DXA scan of the lumbar spine (L1-L4) and femoral neck was performed. All DXA scans were performed using a Hologic Discovery C instrument (Hologic Inc., Bedford, Massachusetts, USA). The WHO criteria[14] were used to classify patients as having osteoporosis (T score −2.5 or below) or osteopenia (T score between −1 and −2.5). A low BMD score was defined as a T score of less than −1. We estimated the 10-year major bone fracture risk by FRAX[15]

Chronic kidney disease classification and renal biomarkers

Serum and urinary creatinine (Cr) levels were measured using an L-type Wako CRE·M reagent (Wako Pure Chemical Industries, Ltd., Japan) on Hitachi Labospect® 008 (Hitachi, Japan). The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease study equation, as adjusted for the Japanese population[16]. Proteinuria was measured using an Uropaper® αIII (Eiken Chemical Co., Tokyo, Japan) on CLINITEK Novus® Automated Urine Chemistry Analyzer (Siemens Healthcare Diagnostics GmbH, Marburg, Germany). The estimated glomerular filtration rate and proteinuria were measured in at least two consecutive analyses that were conducted 3 months apart. Chronic kidney disease was diagnosed according to the guidelines of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI)[17]. Renal tubular function was assessed based on the fractional excretion of phosphate (FEPO$_4$) using

the following equation : (urine PO$_4$/serum creatinine)/(serum PO$_4$/urine creatinine).   Urinary α1 microglobulin was measured using enzyme-linked immunosorbent assay (ELISA) kits (LZ Test Eiken α 1-M ; Eiken Chemical Co., Tokyo, Japan).   The concentration of urinary α1 microglobulin was standardized to a urinary Cr of 1 g/L (/gCr).   All of the laboratory tests of this study were analyzed in the central clinical laboratory of our hospital or SRL Hachioji Laboratory, both of which have the accreditations of the ISO 15189.

Statistical analysis

All statistical tests were 2-sided, with a threshold of 5%.   Continuous variables are reported using medians and interquartile ranges, except when stated otherwise.   Categorical variables are reported using numbers and percentages.   The chi-square test was used to compare categorical variables between the two groups.   A non-parametric Mann-Whitney U test was performed to compare continuous variables.   Logistic regression was used to determine factors associated with low BMD.   All variables with a P-value of < 0.1 in the univariate analysis were entered in a multivariate logistic model.   Correlations between the various renal markers and BMD values were assessed using the Spearman correlation coefficient.   Statistical analysis was performed using SPSS software, version 22.0 (SPSS, Chicago, IL).

Results

Cohort characteristics

Among the 536 HIV-positive patients who were 40 years or older, 228 were excluded due to lack of DXA scan data.   Two more who only underwent a DXA scan at one of the two sites were also excluded (Fig. 1).   The baseline characteristics of the 306 participants are shown in Table 1.   Median age was 49 [(interquartile range [IQR], 46-55)] years ; 96.4% of the participants were Japanese, and 95.1% were men.   Ninety-six percent of the patients received antiretroviral therapy.   Among these, 93.6% achieved a HIV-1 viral load less than 50 copies/mL, 53.0% were using TDF-contained therapy, and 33.0% were using PI/r as part of their regimen.   The current and nadir median CD4 cell counts were 520 cells/μL and 161 cells/μL, respectively.   Regarding conventional risk factors for osteoporosis, 40.2% of the patients were current smokers, and 10.1% consumed more than 3 units of alcohol/day.   Sixteen percent of the patients had a BMI score of less than 20 kg/m^2.   Ten (3.3%) patients were treated with corticosteroids, and 10.8% had a history of prior bone fracture.   The prevalence of comorbidities was as follows : hypertension (29.7%), DM (10.8%), dyslipidemia (20.9%), CKD (21.9%), and CVD (2.9%).   Further details of the demographic characteristics, laboratory profiles, and antiretroviral regimens and duration are summarized in Table 1.
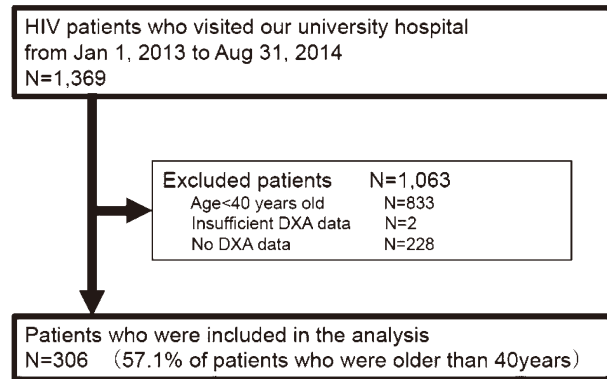
Fig. 1   Flow chart of study population selection.
Total of 1,369 HIV patients visited our university hospital between Jan 1, 2013 and Aug 31, 2014.   1,063 patients were excluded (age < 40 years, 833 ; insufficient DXA, 2 ; no DXA, 228). Total of 306 patients were included in analysis.

Prevalence of BMD Loss

Forty-five percent of the patients showed low BMD (37.9% osteopenia, 7.2% osteoporosis) at the lumbar spine, and 55.2% of the patients showed low BMD (48.7% osteopenia, 6.5% osteoporosis) at the femoral neck.   The prevalence of osteoporosis and osteopenia according to the age groups was relatively stable at the lumbar spine but increased at the femoral neck with age (Table 2).   The prevalence of low BMD among patients aged 40 to 49 years was 44.8% at the lumbar spine and 50.4% at the femoral neck.   The analysis of the two groups, normal or low BMD, is shown in Table 3.

Risk factors for BMD loss

The distribution of T scores at the lumbar spine and femoral neck according to CKD status is shown in Fig 2.   In univariate logistic regression models (Table 4), low BMD at the lumbar spine was correlated with lower BMI, longer PI/r duration, and the absence of DM.   In the multivariate logistic regression model, only PI/r duration was significantly correlated with low BMD at the lumbar spine (Odds ratio [OR] per year increase, 1.088 ; 95% CI 1.023-1.158) after adjusting for BMI, smoking, and DM.   In univariate logistic regression models, low BMD at the femoral neck was correlated with age, lower BMI, smoking, CKD and longer PI/r duration.   In the multivariate logistic regression model, lower BMI (OR per 1.0 increase, 0.880 ; 95% CI 0.819-0.945), smoking (OR 2.078 ; 95% CI 1.251-3.452), CKD (OR 1.999 ; 95% CI 1.078-3.812) and longer PI/r duration (OR per 1 year increase, 1.089 ; 95% CI 1.013-1.171) were correlated with low BMD at the femoral neck after adjusting for age, nadir CD4, and TDF exposure duration.   The duration of TDF and other classical risk factors, such as prior fracture, use of steroids, and alcohol consumption, were not correlated with low

Table 1　Baseline characteristics of study patients.

Patient characteristics (N=306)	Number of patients (%) or median [IQR]
Age, years	49 [46, 55]
Men	291 (95.1)
Japanese	295 (96.4)
Body mass index	23.3 [21.2, 25.0]
Hemophilia, blood coagulation disorders	13 (4.2)
Any history of fractures	33 (10.8)
Familial history of fracture	5 (1.6)
Corticosteroid use	10 (3.3)
Rheumatic disorder	1 (0.3)
Hypertension (+)	91 (29.7)
Diabetes mellitus (+)	33 (10.8)
Dyslipidemia (+)	64 (20.9)
Chronic kidney disease (+)	67 (21.9)
Cardiovascular disease (+)	9 (2.9)
Current smoking	123 (40.2)
Alcohol intake (more than 3 units/day)	31 (10.1)
Hepatitis B surface antigen positive	8 (2.6)
Hepatitis C antibody positive	18 (5.9)
Current CD4 cell count, (cells/μL)	520 [368, 695]
Nadir CD4 cell count, (cells/μL)	161 [47, 256]
Log HIV-RNA (logcopies/mL)	0 [0, 1.28]
HIV-RNA < 50 copies/mL	280 (91.5)
eGFR, mL/min/1.73 m^2	77.0 [66.8, 87.7]
eGFR less than 60 mL/min/1.73 m^2	44 (14.4)
eGFR grade 1	60 (19.6)
eGFR grade 2	202 (66.0)
eGFR grade 3a	37 (12.1)
eGFR grade 3b	5 (1.6)
eGFR grade 4	1 (0.3)
eGFR grade 5	1 (0.3)
Proteinuria	37 (12.1)
Phosphate wasting	21 (6.9)
Current use of ART	294 (96.1)
ART exposure (years)	6.23 [2.72, 11.1]
TDF exposure (years)	1.94 [0, 5.4]
PI/r exposure (years)	0 [0, 5.16]
Current use of PI/r	102 (33.0)
Current use of TDF	162 (53.0)
Current use of ABC	102 (36.0)

Values are expressed as medians [IQR] or as numbers (%).　ART, antiretroviral therapy ;
BMI, body mass index.　Time on tenofovir (years).　CV, coefficient of variation.

BMD.

Renal biomarkers and femoral bone mineral density loss

In a bivariate correlation (Table 5), the T score at the femoral neck showed the best correlation with BMI (r_s = 0.265, P < 0.001), and the T score at the lumbar spine showed the best inverse correlation with PI/r duration (r_s = −0.221, P < 0.010).　No significant correlation was observed between femoral neck low BMD and eGFR (r_s = −0.078, P = 0.171), FEPO$_4$ (r_s = −0.082, P = 0.153), or urinary α1 microglobulin (r_s = −0.121, P = 0.054).　No single factor showed a relationship with low BMD at the femoral neck or renal markers.

Discussion

Prevalence of BMD loss and osteoporosis

The present results revealed that bone mineral density loss was prevalent among elderly Japanese HIV patients.

Table 2　Prevalence of osteopenia and osteoporosis according to WHO criteria of DEXA scan on (A) lumber spine and (B) femoral neck in each age group.

(A) lumber spine

Age group (years)		40-49	50-59	60-69	70-	Total
Normal	*n* (%)	79(55.2)	63(54.3)	22(57.9)	4(44.5)	168(54.9)
Osteopenia	*n* (%)	55(38.5)	48(41.4)	10(26.3)	3(33.3)	116(37.9)
Osteoporosis	*n* (%)	9(6.3)	5(4.3)	6(15.8)	2(22.2)	22(7.2)
Total	*n* (%)	143(100)	116(100)	38(100)	9(100)	306(100)

(B) femoral neck

Age group (years)		40-49	50-59	60-69	70-	Total
Normal	*n* (%)	71(49.7)	51(44.0)	13(34.2)	2(22.2)	137(44.8)
Osteopenia	*n* (%)	63(44.0)	62(53.4)	21(55.3)	3(33.3)	149(48.7)
Osteoporosis	*n* (%)	9(6.3)	3(2.6)	4(10.5)	4(44.5)	20(6.5)
Total	*n* (%)	143(100)	116(100)	38(100)	9(100)	306(100)
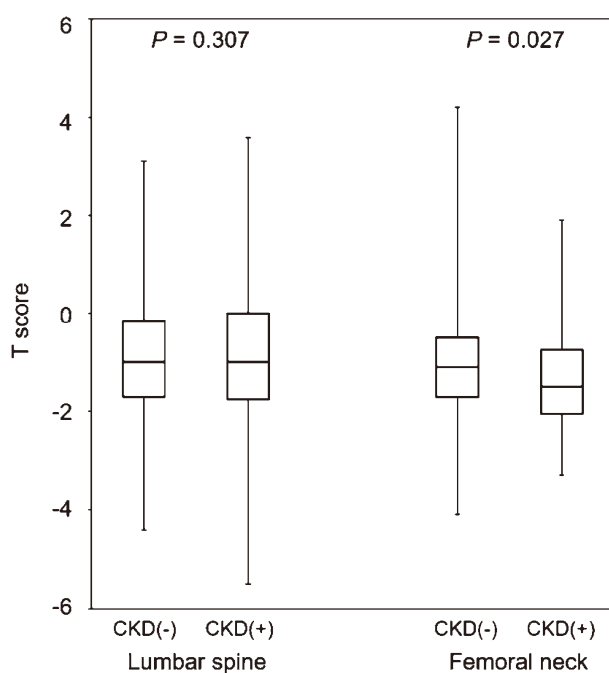
Fig. 2　Boxplot of data from T-scores at lumbar spine and femoral neck with or without chronic kidney disease.
T-scores in patients with CKD were lower than those in patients without CKD at femoral neck (*P*=0.027).

Prevalence was higher among the older patient groups, although the group the 40s age group also showed a high prevalence of osteoporosis compared with the general Japanese population[18] at both the lumbar spine and femoral neck. This trend was especially prominent among patients aged younger than 50 years. The prevalence of osteoporosis in patients with HIV was 6.3% in the 40s age group, whereas it was only 0% in the general Japanese population in the same age group[18]. More than half of HIV-infected patients show low BMD based on several international cohorts, although the percentage varies depending on age and sex[4)19]. The prevalence of low BMD in HIV-infected patients has been reported to range between 27% and 62.7% in the USA[20)21], 16.7% and 54.8% in Korea[22)23], and 55% and 66% in Japan[24)25], and be 39.4% in Taiwan[26]. The present results are in concordance with those of these earlier studies, indicating the importance of BMD evaluation in Japanese HIV-infected patients, even those of the younger generation.

Recommendation for use of DXA scan

The Infectious Diseases Society of America, the European AIDS Clinical Society and other HIV and bone experts recommend DXA screening in HIV-infected postmenopausal women and men of age 50 years or older[27]. The Osteo Renal Exchange Program recently added to these recommendations by including HIV-infected men aged 40-49 years or premenopausal women age greater than 40 years with a Fracture Risk Assessment Tool (FRAX) score of more than 10% regarding 10-year risk of major osteoporotic facture, and did not routinely recommend DXA among those aged 40-49 years[9]. In the present study, none of the patients with a low BMD aged 40-49 years met the recommendation based on FRAX, even when including HIV infection as a secondary risk factor (data not shown). Such guidelines should consider the heightened risk of bone loss in younger HIV-infected patients. In an HIV Outpatient Study, HIV patients older than 47 years had increased fracture risk, even after adjusting for multiple factors[28]. We recommend that all HIV patients over 40 years should receive a DXA scan at least once. Therefore, we need to be vigilant regarding the real risk of fracture among HIV-infected patients[29].

Importance of classical risk factors

The present results confirmed the importance of classical risk factors for bone loss, such as smoking and a low BMI score. Our cohort showed a high prevalence

Table 3 Patient characteristics according to presence or absence of low bone mineral density.

Patient characteristic (* ; P<0.05 : L,F)	Lumbar spine			Femoral neck		
	Normal (n=168)	Low BMD (n=138)	P for trend	Normal (n=137)	Low BMD (n=169)	P for trend
Age, years (,*)	49 [45, 54]	49 [45, 55]	0.902	49 [45, 53]	51 [46, 57]	0.02
Men, no. (%)	159 (94.6)	132 (95.7)	0.793	127 (92.7)	164 (97.0)	0.11
Japanese, no. (%)	161 (95.8)	134 (97.1)	0.76	129 (92.7)	166 (98.2)	0.069
Body mass index (*,*)	23.6 [21.8, 25.8]	22.8 [20.3, 25.1]	0.023	24.0 [21.9, 26.6]	22.9 [20.7, 24.8]	0.001
Hemophilia, coagulation disorders, no. (%)	7 (4.2)	6 (4.3)	1	3 (2.2)	10 (5.9)	0.154
HIV-RNA <50 copies/mL, no. (%)	152 (90.5)	128 (92.8)	0.541	121 (88.3)	159 (94.1)	0.098
Current CD4+ cell count (cells/μL)	531.2 [396.7, 720.4]	509.7 [341.8, 674.7]	0.194	535 [402, 702]	506 [341, 691]	0.226
nadir CD4 cell count, (cells/μL) (,*)	167 [66.9, 269.2]	146.9 [37.5, 246.8]	0.268	183 [90, 267]	126 [31, 251]	0.006
Any history of fracture, no. (%)	15 (8.9)	18 (13.0)	0.27	14 (10.2)	19 (11.2)	0.854
Familial history of fracture, no. (%)	4 (2.4)	1 (0.7)	0.383	4 (2.9)	1 (0.5)	0.177
Corticosteroid use, no. (%)	6 (3.6)	4 (2.9)	1	2 (1.5)	8 (4.7)	0.194
Rheumatic disorder, no. (%)	1 (0.6)	0	1	0	1 (0.6)	1
Hypertension (+) no. (%)	55 (32.7)	36 (26.1)	0.212	40 (29.2)	51 (30.2)	0.9
Diabetes Mellitus (+) no. (%) (*,)	24 (14.3)	9 (6.5)	0.04	18 (13.1)	15 (8.9)	0.268
Chronic Kidney Disease (+) no. (%) (,*)	37 (22.0)	30 (21.7)	1	21 (15.3)	46 (27.2)	0.013
Dyslipidemia (+) no. (%)	32 (19.0)	32 (23.2)	0.399	25 (18.2)	39 (23.1)	0.325
Cardiovascular disease (+) no. (%)	4 (2.4)	0	0.736	4 (2.9)	5 (3.0)	1
Current smoking, no. (%) (,*)	60 (35.7)	63 (45.7)	0.08	44 (32.1)	79 (46.8)	0.01
Alcohol intake (more than 3 units/day), no. (%)	16 (9.5)	15 (10.9)	0.707	12 (8.8)	19 (11.2)	0.569
HBs antigen positive, no. (%)	6 (3.6)	2 (1.4)	0.302	4 (2.9)	4 (2.4)	1
HCV antibody positive, no. (%)	10 (6.0)	8 (5.8)	1	6 (4.4)	12 (7.1)	0.341
eGFR, mL/min/1.73 m^2	75.5 [66.3, 87.7]	78.9 [67.7, 88.2]	0.36	75.3 [66.0, 87.7]	78.8 [67.6, 88.3]	0.362
Proteinuria, no. (%) (,*)	22 (13.1)	15 (10.9)	0.6	11 (8.0)	26 (15.3)	0.036
FEPO$_4$, (%)	10.8 [7.6, 14.1]	11.1 [7.4, 15.3]	0.514	10.4[7.2, 13.9]	11.7 [7.5, 14.9]	0.098
Urinary α1 microglobulin (mg/gCr) (,*)	87.1 [49.8, 147.8]	97.4 [56.7, 152.4]	0.228	84.8 [48.1, 126.4]	97.9 [56.3, 172.0]	0.037
Current use of ART, no. (%)	164 (97.6)	135 (97.8)	1	133 (97.1)	166 (98.2)	0.704
ART exposure (years)	6.5 [2.9, 11.4]	5.7 [2.2, 10.7]	0.201	4.9 [2.5, 10.7]	6.9 [3.0, 11.2]	0.312
TDF exposure (years)	2.1 [0, 5.5]	1.8 [0, 5.4]	0.826	1.5 [0, 5.8]	2.8 [0, 5.9]	0.075
PI/r exposure (years) (*,*)	0 [0, 3.8]	1.0 [0, 6.4]	0.019	0 [0, 3.7]	1.4 [0, 6.3]	0.011
Current use of TDF	85 (50.6)	77 (55.8)	0.421	71 (51.8)	91 (53.8)	0.731
Current use of PI/r (,*)	50 (30.0)	52 (38.0)	0.146	36 (26.3)	66 (39.1)	0.021

Values are expressed as medians [IQR] or as numbers (%). Low bone mineral density is defined as T score of less than −1. Chi-square test was used for categorical variables.

of current smokers. Smoking cessation is also highly recommended for preventing osteoporosis. Alcohol intake was confirmed by patient declaration, so it is possible that the exact level of consumption was underestimated. Alcohol and substance abuse are important risk factors for osteoporosis and fracture[7], although the present study does not provide any information regarding them. Infection with HCV was not related to low BMD according to this study. Compared with previous reports from Europe and America[28)30)], the low prevalence of HCV co-infection among the present cohort (5.9%) may have led to the statistical insignificance observed in this analysis. The results revealed that DM was related to a higher BMD score at the lumbar spine. A meta-analysis confirmed that type2 diabetes patients have a higher BMD score than the non-diabetic population[31], although type 2 DM patients have a higher risk of bone fracture, despite their higher BMD scores[32]. It is estimated that other factors, such as bone quality, are also important for evaluating risk of fracture in DM patients.

Chronic kidney disease-mineral and bone disorder

To our knowledge, this is the first study to demonstrate the existence of a bone-kidney axis among Asian HIV-infected patients. There are several reports on the relationship between CKD and BMD loss among the general population. Chronic kidney disease–mineral and bone disorder (CKD-MBD) is a well-known bone-related complication that is regarded as a late-stage renal complication. Kidney Disease Improving Global Outcomes (KDIGO) stated in their guidelines[33] that BMD measurement is not routinely recommended for CKD patients because of uncertainty concerning the utility of DXA in CKD. However, recent studies have noted that CKD patient bone loss and fracture are determined at the early stage of CKD[13)34]. Several studies indicate that BMD is low in pre-dialysis and dialysis patients with fractures at the lumbar spine and femoral neck[35)36]. Both low eGFR and higher albuminuria are significant risk factors for fracture[37]. Chronic kidney disease patients should be evaluated for BMD, even during the early stages of the disease. A low eGFR level has been associated with

Table 4   Results of logistic regression analysis of low bone mineral density at each site : (A) lumbar spine, (B) femoral neck.

(A) Lumbar spine

Characteristic	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age, per year	1.003 (0.974-1.034)	0.823		
Hemophilia	1.045 (0.343-3.186)	0.938		
Body mass index	0.935 (0.877-0.995)	0.036	0.951 (0.891-1.016)	0.134
Nadir CD4 cell count (cells/μL)	0.999 (0.997-1.001)	0.291		
log HIV-RNA level (copies/mL)	0.961 (0.778-1.187)	0.712		
Smoking (+)	1.367 (0.990-1.888)	0.058	1.601 (0.993-2.582)	0.054
Alcohol intake	1.168 (0.555-2.457)	0.682		
Hypertension (+)	0.725 (0.441-1.193)	0.206		
Diabetes mellitus (+)	0.419 (0.188-0.934)	0.033	0.438 (0.190-1.009)	0.053
Dyslipidemia (+)	1.283 (0.739-2.228)	0.376		
CKD (+)	0.983 (0.570-1.696)	0.952		
ART exposure, per year	0.969 (0.928-1.013)	0.164		
PI/r exposure, per year	1.074 (1.011-1.141)	0.02	1.088 (1.023-1.158)	0.008
TDF exposure, per year	0.999 (0.935-1.068)	0.983		

(B) Femoral neck

Characteristic	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age, per year	1.042 (1.010-1.076)	0.01	1.035 (0.999-1.072)	0.056
Hemophilia	2.809 (0.758-10.417)	0.122		
Body mass index	0.875 (0.818-0.936)	<0.001	0.880 (0.819-0.945)	<0.001
Nadir CD4 cell count (cells/μL)	0.998 (0.997-1.000)	0.033	1.000 (0.998-1.001)	0.706
log HIV-RNA level (copies/mL)	0.927 (0.751-1.143)	0.476		
Smoking (+)	1.328 (0.621-2.843)	0.01	2.078 (1.251-3.452)	0.005
Alcohol intake	1.328 (0.621-2.843)	0.465		
Hypertension (+)	1.048 (0.640-1.717)	0.852		
Diabetes mellitus (+)	0.644 (0.312-1.331)	0.235		
Dyslipidemia (+)	1.344 (0.766-2.358)	0.303		
CKD (+)	2.066 (1.162-3.672)	0.013	1.999 (1.078-3.812)	0.035
ART exposure, per year	1.017 (0.974-1.063)	0.443		
PI/r exposure, per year	1.094 (1.027-1.166)	0.005	1.089 (1.013-1.171)	0.021
TDF exposure, per year	1.062 (0.992-1.136)	0.085	1.051 (0.972-1.136)	0.209

CKD, chronic kidney disease ; ART, antiretroviral therapy ; PI/r, ritonavir-boosted protease inhibitor ; TDF, tenofovir disoproxil fumarate ; OR, odds ratio ; CI, confidence interval Low bone mineral density was defined as T score of less than −1.

increased risk of fracture[38]. The mechanism of CKD and BMD loss has not been clearly established. Several explanations have been proposed, including changes related to a spectrum of disorders in bone turnover, mineralization or volume that are linked to vascular calcification, hyperphosphatemia, and hyperparathyroidism[39].

Secondary osteoporosis is of increasing concern among HIV-infected patients. Casado *et al*.[40] reported that CKD is an independent risk factor for osteoporosis among HIV-infected patients. The present study confirmed that CKD is an independent risk factor for low BMD at the femoral neck. Among renal factors, eGFR and FEPO$_4$ were not significantly correlated with bone loss. Creatinine-based eGFR is influenced not only by kidney function, but also by muscle mass, which is an important determinant of fracture risk[41] ; therefore, other renal markers, such as cystatin C, may be better able to predict fracture risk[42]. Urinary α1 microglobulin was statistically significant, but this relationship was very weak. However, urinary α1 microglobulin is a risk factor for the development of tubular toxicity[43], and it is possible that proximal tubular dysfunction may be related

Table 5　Correlation of baseline and renal parameters with T score at each site.

	T score at lumbar spine	P-value	T score at femoral neck	P-value
Age (years)	0.007	0.902	-0.148	0.01
BMI (kg/m^2)	0.181	0.001	0.265	<0.001
Nadir CD4 (cells/μL)	0.087	0.128	0.182	0.001
eGFR (mL/min/1.73 m^2)	-0.107	0.061	-0.078	0.171
FEPO$_4$ (%)	-0.039	0.497	-0.082	0.153
urinary α1 microglobulin (mg/gCr)	-0.073	0.202	-0.121	0.054
ART duration (years)	0.02	0.733	-0.075	0.191
TDF duration (years)	-0.039	0.496	-0.058	0.314
PI/r duration (years)	-0.221	<0.001	-0.178	0.002

BMI, body mass index ; eGFRcr, estimated glomerular filtration rate ; FEPO$_4$, fractional excretion of phosphate ; ART, antiretroviral therapy ; PI/r, ritonavir-boosted protease inhibitor ; TDF, tenofovir disoproxil fumarate

to both bone loss and CKD through the same pathogenesis mechanism, such as inflammation induced by immune reconstitution. The CKD criteria are formulated based on a combination of eGFR and proteinuria to precisely predict renal prognosis ; therefore, it may be more accurate to evaluate the risk of bone loss among CKD patients than using any of the single renal markers that were evaluated in this study.

Several studies have shown that TDF is correlated with bone loss among HIV-infected and non-HIV infected patients. It is supposed that TDF induces hypophosphatemia secondary to proximal renal tubular dysfunction, resulting in bone reabsorption, in an attempt to liberate matrix phosphorus[44]. However, the present results revealed that femoral neck bone loss was not related to FEPO$_4$ or TDF duration. Avoidance of TDF use among CKD or phosphate-wasting patients might affect this result. Increased protease inhibitor use was consistently related to bone loss at both the lumbar spine and the femoral neck, as reported previously[25][45].

Early start of antiretroviral therapy has been universally recommended in recent years[46]. The direct influence of HIV on bone loss is manageable only when antiretroviral therapy is started early. Furthermore, recent guidelines recommend using integrase inhibitors rather than protease inhibitors ; the less toxic tenofovir prodrug, tenofovir alafenamide, is available in many countries[46], and these ARVs have been shown to be more bone-protective than TDF or PI/r[47][48]. Bone loss induced in response to some specific ARVs will also be minimized in the near future. In this context, the effective management of lifestyle risk factors, including smoking and long-term comorbidities such as CKD, should be emphasized in order to prevent fracture and other complications. Future forecast in the Netherlands estimates that 84% of HIV-infected patients will have at least one non-communicable disease in 2030[49]. A Denmark cohort study showed a higher mortality among HIV

patients with some complications. We should be prepared to control these long-term complications through early evaluation and intervention in high-risk populations among HIV-infected patients.

Limitations

Our study has several limitations. The first being that the large majority of Japanese patients with HIV infection are men. In a report on AIDS issued by the Ministry of Health, Labour and Welfare in Japan, 2017, the number of women with HIV was only 43 (3.6%). Therefore, it is difficult to analyse the gender gap in Japanese patients with HIV infection. Second, this retrospective study was conducted at a single center, and not all the patients were surveyed ; thus, selection bias of the study patients cannot be ruled out. Only 57% of the population was evaluated because DXA scans are not routinely performed in general practice here, especially in the younger generation. Third, because of the retrospective design of the study, a causal relation is uncertain. The possibility exists that the same pathogenesis, such as chronic inflammation induced by HIV infection, might have played an important role in both BMD loss and renal dysfunction. Further studies are needed to confirm the relations defining the bone-renal axis among HIV-infected patients and to determine the pathogenesis of this phenomenon. Finally, despite having adjusted for multiple potential risk factors, we cannot exclude possible residual confounding factors, such as hyperparathyroidism, hypogonadism, low vitamin D levels, and immobility. However, the present study used blood and urine test results obtained on routine visits. The insights provided by our study might be widely applicable to many clinical settings.

Conclusions

The present analysis revealed a high prevalence of bone loss, especially at the femoral neck, in all age

groups, including among patients aged 40 years or more. Chronic kidney disease was found to be an independent risk factor for a low BMD score at the femoral neck. Further screening based on DXA scanning is needed to detect osteopenia and osteoporosis among HIV-infected patients, especially those with CKD. Prospective studies to evaluate the causal relations between BMD loss and CKD pathogenesis among HIV patients are warranted to aid in the detection of future risk of fracture.

Conflict of interest

The authors wish to declare no conflict of interest.

Acknowledgments

References

1) Serrano-Villar S, Gutiérrez F, Miralles C, Berenguer J, Rivero A, Martínez E, Moreno S : Human Immunodeficiency Virus as a Chronic Disease : Evaluation and Management of Nonacquired Immune Deficiency Syndrome-Defining Conditions. Open Forum Infect Dis **3** : ofw097, 2016

2) Ioannidis G, Papaioannou A, Hopman WM, Akhtar-Danesh N, Anastassiades T, Pickard L, Kennedy CC, Prior JC, Olszynski WP, Davison KS, Goltzman D, Thabane L, Gafni A, Papadimitropoulos EA, Brown JP, Josse RG, Hanley DA, Adachi JD : Relation between fractures and mortality : results from the Canadian Multicentre Osteoporosis Study. CMAJ **181** : 265-271, 2009

3) Marshall D, Johnell O, Wedel H : Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ **312**(7041) : 1254-1259, 1996

4) Brown TT, Qaqish RB : Antiretroviral therapy and the prevalence of osteopenia and osteoporosis : a meta-analytic review. AIDS **20** : 2165-2174, 2006

5) Triant VA, Brown TT, Lee H, Grinspoon SK : Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab **93** : 3499-3504, 2008

6) Fausto A1, Bongiovanni M, Cicconi P, Menicagli L, Ligabò EV, Melzi S, Bini T, Sardanelli F, Cornalba G, Monforte Ad : Potential predictive factors of osteoporosis in HIV-positive subjects. Bone **38** : 893-897, 2006

7) Borderi M, Gibellini D, Vescini F, De Crignis E, Cimatti L, Biagetti C, Tampellini L, Re MC : Metabolic bone disease in HIV infection. AIDS **23** : 1297-310, 2009

8) Stellbrink HJ, Orkin C, Arribas JR, Compston J, Gerstoft J, Van Wijngaerden E, Lazzarin A, Rizzardini G, Sprenger HG, Lambert J, Sture G, Leather D, Hughes S, Zucchi P, Pearce H ; ASSERT Study Group : Comparison of changes in bone density and turnover with abacavir-lamivudine versus tenofovir-emtricitabine in HIV-infected adults : 48-week results from the ASSERT study. Clin Infect Dis **51** : 963-972, 2010

9) Brown TT, Hoy J, Borderi M, Guaraldi G, Renjifo B, Vescini F, Yin MT, Powderly WG : Recommendations for evaluation and management of bone disease in HIV. Clin Infect Dis **60** : 1242-1251, 2015

10) Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, Tashima KT, Roland M, Franceschini N, Palella FJ, Lennox JL, Klotman PE, Nachman SA, Hall SD, Szczech LA : Guidelines for the management of chronic kidney disease in HIV-infected patients : recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis **40** : 1559-1585, 2005

11) Yanagisawa N, Muramatsu T, Yamamoto Y, Tsuchiya K, Nitta K, Ajisawa A, Fukutake K, Ando M : Classification of human immunodeficiency virus-infected patients with chronic kidney disease using a combination of proteinuria and estimated glomerular filtration rate. Clin Exp Nephrol **18** : 600-605, 2014

12) Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY : Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med **351** : 1296-1305, 2004

13) Dooley AC, Weiss NS, Kestenbaum B : Increased risk of hip fracture among men with CKD. Am J Kidney Dis **51** : 38-44, 2008

14) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. WHO technical report series 843. WHO, Geneva, 1-129, 1994

15) Centre for Metabolic Bone Diseases, University of Sheffield, UK. Fracture Risk Assessment Tool. Available from : https://www.sheffield.ac.uk/FRAX/

16) Matsuo S1, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H, Hishida A ; Collaborators developing the Japanese equation for estimated GFR : Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis **53** : 982-992, 2009

17) KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl (2011) **3** : 1-150, 2013

18) Yoshimura N, Muraki S, Oka H, Mabuchi A, En-Yo Y, Yoshida M, Saika A, Yoshida H, Suzuki T, Yamamoto S, Ishibashi H, Kawaguchi H, Nakamura K, Akune T :

Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women : the research on osteoarthritis/osteoporosis against disability study.　J Bone Miner Metab **27** : 620-628, 2009

19) Cazanave C, Dupon M, Lavignolle-Aurillac V, Barthe N, Lawson-Ayayi S, Mehsen N, Mercié P, Morlat P, Thiébaut R, Dabis F ; Groupe d'Epidémiologie Clinique du SIDA en Aquitaine : Reduced bone mineral density in HIV-infected patients : prevalence and associated factors.　AIDS **22** : 395-402, 2008

20) Arnsten JH, Freeman R, Howard AA, Floris-Moore M, Santoro N, Schoenbaum EE : HIV infection and bone mineral density in middle-aged women.　Clin Infect Dis **42** : 1014-1020, 2006

21) Brown TT, Ruppe MD, Kassner R, Kumar P, Kehoe T, Dobs AS, Timpone J : Reduced bone mineral density in human immunodeficiency virus-infected patients and its association with increased central adiposity and postload hyperglycemia.　J Clin Endocrinol Metab **89** : 1200-1206, 2004

22) Choe PG, Choi HJ, Kim NH, Park WB, Song KH, Bang JH, Kim ES, Park SW, Kim HB, Oh MD, Kim NJ : High prevalence of low bone mass and associated factors in Korean HIV-positive male patients undergoing antiretroviral therapy.　J Int AIDS Soc **17** : 18773, 2014

23) Kim HS, Chin BS, Shin HS : Prevalence and risk factors of low bone mineral density in Korean HIV-infected patients : impact of abacavir and zidovudine. J Korean Med Sci **28** : 827-832, 2013

24) Kinai E, Nishijima T, Mizushima D, Watanabe K, Aoki T, Honda H, Yazaki H, Genka I, Tanuma J, Teruya K, Tsukada K, Gatanaga H, Kikuchi Y, Oka S : Long-term use of protease inhibitors is associated with bone mineral density loss.　AIDS Res Hum Retroviruses **30** : 553-559, 2014

25) Koga I, Yoshino Y, Kitazawa T, Kurahashi I, Ota Y : Prevalence and risk factors for loss of bone mineral density in male Japanese patients with HIV.　J Acquir Immune Defic Syndr **62** : e25-27, 2013

26) Tsai MS, Hung CC, Liu WC, Chen KL, Chen MY, Hsieh SM, Sheng WH, Sun HY, Shih TT : Reduced bone mineral density among HIV-infected patients in Taiwan : prevalence and associated factors.　J Microbiol Immunol Infect **47** : 109-115, 2014

27) Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA ; Infectious Diseases Society of America : Primary care guidelines for the management of persons infected with HIV : 2013 update by the HIV medicine association of the Infectious Diseases Society of America.　Clin Infect Dis **58** : e1-34, 2014

28) Young B, Dao CN, Buchacz K, Baker R, Brooks JT ; HIV Outpatient Study (HOPS) Investigators : Increased rates of bone fracture among HIV-infected persons in the HIV Outpatient Study (HOPS) compared with the US general population, 2000-2006.

Clin Infect Dis **52** : 1061-1068, 2011

29) Yin MT, Shiau S, Rimland D, Gibert CL, Bedimo RJ, Rodriguez-Barradas MC, Harwood K, Aschheim J, Justice AC, Womack JA : Fracture Prediction With Modified-FRAX in Older HIV-Infected and Uninfected Men.　J Acquir Immune Defic Syndr **72** : 513-520, 2016

30) Collin F, Duval X, Le Moing V, Piroth L, Al Kaied F, Massip P, Villes V, Chêne G, Raffi F ; ANRS CO8 APROCO-COPILOTE study group : Ten-year incidence and risk factors of bone fractures in a cohort of treated HIV1-infected adults.　AIDS **23** : 1021-1024, 2009

31) Ma L, Oei L, Jiang L, Estrada K, Chen H, Wang Z, Yu Q, Zillikens MC, Gao X, Rivadeneira F : Association between bone mineral density and type 2 diabetes mellitus : a meta-analysis of observational studies.　Eur J Epidemiol **27** : 319-332, 2012

32) Giangregorio LM, Leslie WD, Lix LM, Johansson H, Oden A, McCloskey E, Kanis JA : FRAX underestimates fracture risk in patients with diabetes.　J Bone Miner Res **27** : 301-308, 2012

33) Kidney Disease : Improving Global Outcomes (KDIGO) CKD-MBD Work Group : KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD).　Kidney Int Suppl **113** : S1-130, 2009

34) Ensrud KE, Lui LY, Taylor BC, Ishani A, Shlipak MG, Stone KL, Cauley JA, Jamal SA, Antoniucci DM, Cummings SR ; Osteoporotic Fractures Research Group : Renal function and risk of hip and vertebral fractures in older women.　Arch Intern Med **167** : 133-139, 2007

35) Bucur RC, Panjwani DD, Turner L, Rader T, West SL, Jamal SA : Low bone mineral density and fractures in stages 3-5 CKD : an updated systematic review and meta-analysis.　Osteoporos Int **26** : 449-458, 2015

36) Jamal SA, Hayden JA, Beyene J : Low bone mineral density and fractures in long-term hemodialysis patients : a meta-analysis.　Am J Kidney Dis **49** : 674-681, 2007

37) Daya N, Voskertchian A, Schneider ALC, Ballew S, McAdams DeMarco M, Coresh J, Appel LJ, Selvin E, Grams ME : Kidney Function and Fracture Risk : The Atherosclerosis Risk in Communities (ARIC) Study.　Am J Kidney Dis **67** : 218-226, 2016

38) Fried LF, Biggs ML, Shlipak MG, Seliger S, Kestenbaum B, Stehman-Breen C, Sarnak M, Siscovick D, Harris T, Cauley J, Newman AB, Robbins J : Association of kidney function with incident hip fracture in older adults.　J Am Soc Nephrol **18** : 282-286, 2007

39) Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, Ott S, Sprague S, Lameire N, Eknoyan G ; Kidney Disease : Improving Global Outcomes (KDIGO) : Definition, evaluation, and

classification of renal osteodystrophy : a position statement from Kidney Disease : Improving Global Outcomes (KDIGO).　Kidney Int **69** : 1945-1953, 2006

40) Casado JL, Bañon S, Andrés R, Perez-Elías MJ, Moreno A, Moreno S : Prevalence of causes of secondary osteoporosis and contribution to lower bone mineral density in HIV-infected patients.　Osteoporos Int **25** : 1071-1079, 2014

41) Odden MC, Shlipak MG, Tager IB : Serum creatinine and functional limitation in elderly persons.　J Gerontol A Biol Sci Med Sci **64** : 370-376, 2009

42) Ensrud KE, Parimi N, Fink HA, Ishani A, Taylor BC, Steffes M, Cauley JA, Lewis CE, Orwoll ES ; Osteoporotic Fractures in Men Study Group : Estimated GFR and risk of hip fracture in older men : comparison of associations using cystatin C and creatinine.　Am J Kidney Dis **63** : 31-39, 2014

43) Jotwani V, Scherzer R, Estrella MM, Jacobson LP, Witt MD, Palella FJ Jr, Macatangay B, Bennett M, Parikh CR, Ix JH, Shlipak MG : HIV Infection, Tenofovir, and Urine α1-Microglobulin : A Cross-sectional Analysis in the Multicenter AIDS Cohort Study.　Am J Kidney Dis **68** : 571-581, 2016

44) Taiwo BO, Chan ES, Fichtenbaum CJ, Ribaudo H, Tsibris A, Klingman KL, Eron JJ, Berzins B, Robertson K, Landay A, Ofotokun I, Brown T ; AIDS Clinical Trials Group A5303 Study Team : Less Bone Loss With Maraviroc- Versus Tenofovir-Containing Antiretroviral Therapy in the AIDS Clinical Trials Group A5303 Study.　Clin Infect Dis **61** : 1179-1188, 2015

45) Bonjoch A, Figueras M, Estany C, Perez-Alvarez N, Rosales J, del Rio L, di Gregorio S, Puig J, Gómez G, Clotet B, Negredo E ; Osteoporosis Study Group : High prevalence of and progression to low bone mineral density in HIV-infected patients : a longitudinal cohort study.　AIDS **24** : 2827-2833, 2010

46) U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.　Available from : https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

47) Sax PE, Wohl D, Yin MT, Post F, DeJesus E, Saag M, Pozniak A, Thompson M, Podzamczer D, Molina JM, Oka S, Koenig E, Trottier B, Andrade-Villanueva J, Crofoot G, Custodio JM, Plummer A, Zhong L, Cao H, Martin H, Callebaut C, Cheng AK, Fordyce MW, McCallister S ; GS-US-292-0104/0111 Study Team : Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection : two randomised, double-blind, phase 3, non-inferiority trials.　Lancet **385** : 2606-2615, 2015

48) Brown TT, Moser C, Currier JS, Ribaudo HJ, Rothenberg J, Kelesidis T, Yang O, Dubé MP, Murphy RL, Stein JH, McComsey GA : Changes in Bone Mineral Density After Initiation of Antiretroviral Treatment With Tenofovir Disoproxil Fumarate/Emtricitabine Plus Atazanavir/Ritonavir, Darunavir/Ritonavir, or Raltegravir.　J Infect Dis **212** : 1241-1249, 2015

49) Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem Av, de Wolf F, Hallett TB ; ATHENA observational cohort : Future challenges for clinical care of an ageing population infected with HIV : a modelling study.　Lancet Infect Dis **15** : 810-818, 2015

HIV 感染者において慢性腎臓病は大腿骨頸部の骨密度低下に関連する

村 松　　崇　　　天 野 景 裕　　　近 澤 悠 志
備 後 真 登　　　四 本 美 保 子　　　大 瀧　　学
萩 原　　剛　　　福 武 勝 幸

東京医科大学臨床検査医学分野

【要旨】【背景】HIV 感染者では骨密度減少の頻度が高い。しかし、その有病率や危険因子としての古典的な危険因子や HIV 感染者に特有な薬剤や共感染の影響などに関する日本人患者の情報は乏しい。

【方法】我々は単一施設の後方視的研究として、当院外来を 2013 年 1 月から 2014 年 8 月まで受診した HIV 感染者で 40 歳以上であった症例において、二重エネルギー X 線吸収測定法（dual-energy X-ray absorptiometry, DXA）による椎体と大腿骨頸部の骨密度を評価した症例を解析した。骨密度低下の危険因子を評価するため多重ロジスティック回帰分析を行った。腎関連検査との骨密度の関係を評価するため線形回帰分析を行った。

【結果】306 例が該当し年齢の中央値は 49 歳、96.4% が日本人、95.1% が男性で、CD4 陽性リンパ球数の中央値は 520/μL、96.1% の症例で抗ウイルス療法（antiretroviral therapy）が行われていた。椎体での評価では 37.9% が骨減少症、7.2% が骨粗鬆症であり、大腿骨頸部の評価では 48.7% が骨減少症、6.5% が骨粗鬆症であり、40 歳代でも両測定部位で骨粗鬆症が認められた。多重ロジスティック回帰分析では大腿骨頸部の骨密度低下の独立した危険因子として慢性腎臓病（オッズ比 1.999、95% 信頼区間 1.078-3.812）が判明し、従来から海外で指摘されている因子（BMI、喫煙、リトナビル使用）も認められた。

【結語】40 歳以上の HIV 感染者において DXA による評価の必要性が示された。大腿骨頸部においては慢性腎臓病が従来指摘されていた危険因子とは独立した危険因子であることが示された。

〈キーワード〉 HIV 感染症、慢性腎臓病、骨密度低下、骨粗鬆症