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Lower peak bone mass and abnormal trabecular and cortical microarchitecture in young men infected with HIV early in life

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Abstract

Introduction—HIV infection and antiretroviral therapy (ART) early in life may interfere with acquisition of peak bone mass, thereby increasing fracture risk in adulthood.

Methods—We conducted a cross-sectional study of dual-energy X-ray absorptiometry (DXA) and high-resolution peripheral quantitative computed tomography (HR-pQCT) in 30 HIV-infected African-American or Hispanic Tanner stage 5 men aged 20–25 on ART (15 perinatally infected and 15 infected during adolescence) and 15 HIV-uninfected controls.

Results—HIV-infected men were similar in age and BMI, but were more likely to be African-American ($P = 0.01$) than uninfected men. DXA-derived areal bone mineral density (aBMD) Z-scores were 0.4–1.2 lower in HIV-infected men at the spine, hip, and radius (all $P < 0.05$). At the radius and tibia, total and trabecular volumetric BMD (vBMD), and cortical and trabecular thickness were between 6 and 19% lower in HIV-infected than uninfected men ($P < 0.05$). HIV-infected men had dramatic deficiencies in plate-related parameters by individual trabeculae segmentation (ITS) analyses and 14–17% lower bone stiffness by finite element analysis revealed. Differences in most HR-pQCT parameters remained significant after adjustment for race/ethnicity. No DXA or HR-pQCT parameters differed between men infected perinatally or during adolescence.

Conclusion—At an age by which young men have typically acquired peak bone mass, HIV-infected men on ART have lower BMD, markedly abnormal trabecular plate and cortical microarchitecture, and decreased whole bone stiffness, whether infected perinatally or during adolescence. Reduced bone strength in young adults infected with HIV early in life may place them at higher risk for fractures as they age.

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Conflicts of interest

The other authors have no conflicts of interest.

Keywords

bone microarchitecture; bone mineral density; bone strength; high-resolution peripheral quantitative computed tomography; peak bone mass; perinatal HIV infection

Introduction

Children who acquire HIV infection perinatally or in adolescence have the greatest cumulative exposure to potentially adverse effects of HIV infection and/or antiretroviral therapy (ART) on the skeleton. Peak bone mass is a key determinant of osteoporosis and fracture risk later in life [1]. If HIV infection and/or ART interfere with bone acquisition during childhood and adolescence resulting in lower peak bone size and mass, fracture risk may be increased in adulthood. Several cross-sectional studies have found both lower bone mineral content (BMC) and bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) in perinatally HIV-infected children compared with healthy children of similar age and sex [2–5], even after adjustment for stage of sexual maturation, height, and weight [2]. A recent study also found that behaviorally infected adolescent men on antiretrovirals had lower BMD by DXA than uninfected controls [6]. However, a major limitation of DXA is that it does not measure the anteroposterior diameter of bone. Therefore, measurement of areal BMD (aBMD) by DXA may underestimate true volumetric BMD (vBMD) especially in children with impaired growth, delayed pubertal development, and smaller bone size. Notably, the only published study comparing aBMD by DXA and vertebral vBMD by quantitative computed tomography (CT) in HIV-infected and uninfected children and adolescents found discrepant results [7]. No study has yet compared aBMD by DXA and vBMD by CT in HIV-infected and uninfected young adults after peak bone mass has likely been achieved. In addition, DXA cannot distinguish between cortical and trabecular bone, nor can it measure bone microarchitecture, which also influences fracture risk independent of aBMD [8]. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a noninvasive imaging technology that provides a three-dimensional measurement of true vBMD at the distal radius and tibia, and permits separate assessment of cortical and trabecular bone microarchitecture [9,10]. In addition, individual trabeculae segmentation (ITS)-based morphological analysis, a novel analysis technique for HR-pQCT images, can distinguish between trabecular plates, which play the dominant and critical role in mechanical competence of trabecular bone, from trabecular rods, and predict fracture status independently of aBMD [11–13].

We hypothesized that, compared with uninfected controls, individuals infected with HIV early in life would have lower cortical and trabecular vBMD as well as abnormal trabecular and plate and rod microarchitecture, features that are associated with reduced bone strength and prevalent fractures in older men and women who are not infected with HIV [14]. Because perinatally infected men have had longer exposure to both the HIV virus and ART, we also hypothesized that vBMD would be lower and microarchitectural abnormalities more pronounced in perinatally infected men than those infected during adolescence.

Materials and methods

Study participants

Between May and August of 2012, 45 (30 HIV-infected, 15 HIV-uninfected) African-American or Hispanic men, aged 20–25 years and Tanner 5 developmental stage were recruited from the infectious diseases and general internal medicine clinics at Columbia University Medical Center (CUMC) in New York City. HIV-infected men were infected either perinatally ($n = 15$) or during adolescence ($n = 15$) and all were on ART. Exclusion criteria included history of fragility fracture or osteoporosis; metabolic bone disease; multiple myeloma or metastatic cancer; endocrinopathies; serum creatinine more than 1.5 mg/dl; liver, celiac or inflammatory bowel disease; and current glucocorticoid or anticonvulsant use. Fifteen HIV-uninfected controls meeting the same criteria with serostatus verified by enzyme-linked immunosorbent assay were also enrolled from an outpatient clinic within the same health system.

Medical, surgical, and sexual health history, including age of sexual debut, current tobacco and alcohol use, current and past medication history, HIV and ART history, current and nadir CD4⁺ T-cell counts, and HIV-1 plasma RNA levels were obtained by interview and chart review. Eligible participants self-identified their race/ethnicity and developmental stage was determined using self-assessment illustrations [15]. This study was approved by the Institutional Review Board of CUMC and all participants provided written informed consent.

Bone density and body composition measurements

aBMD of the lumbar spine (L1–4), femoral neck, total hip, nondominant 1/3 radius, ultradistal radius (UDR), and body composition were measured by DXA on a QDR 4500 bone densitometer (Hologic Inc., Bedford, Massachusetts, USA) at CUMC. Short-term in-vivo precision is 0.68% for the lumbar spine, 1.36% for the total hip, and 0.70% for the radius. Z-scores, comparing aBMD to an age-matched, sex-matched, and race/ethnicity-matched reference population were derived for the hip from the National Health and Nutrition Examination Survey (NHANES III) and the manufacturer's normative database for the spine and forearm. Height (cm) and weight (kg) were measured by Harpenden stadiometer (Holtain Ltd., Crymych, UK) and balance beam scale, respectively. BMI was calculated as weight divided by squared height (m^2).

High-resolution peripheral quantitative computed tomography measurements

Cross-sectional area (CSA), vBMD, and microarchitecture were assessed at the nondominant distal radius and distal tibia by HR-pQCT (XtremeCT; Scanco Medical, Brüttisellen, Switzerland) as described in detail elsewhere [9,16,17]. Briefly, this system allows for high-resolution in-vivo evaluation of bone structure at a nominal isotropic resolution of 82 μm . The region of interest (ROI) consisted of an approximately 9 mm axial length of bone. At the radius, the ROI was located 9.5–18.5 mm proximal to the endplate. At the tibia, the ROI was located 22–31 mm proximal to the endplate [9,17]. Bone microarchitecture analysis was performed according to the manufacturers' standard evaluation protocol as previously described [9,18,19]. The following parameters were

reported: CSA; total and trabecular bone density (total vBMD, Tb.vBMD; mg hydroxyapatite/cm³); trabecular number (Tb.N; mm⁻¹); thickness (Tb.Th; μ m); and separation (Tb.Sp; μ m). The standard deviation of Tb.Sp (Tb.Sp.SD; μ m) was measured to assess the heterogeneity of the trabecular network.

Cortical analyses

To evaluate the cortical bone structure, a validated autosegmentation method [20,21] was applied to separate the cortical and trabecular compartments and measure cortical porosity (Ct.Po, %), direct cortical thickness (Ct.Th, mm), and cortical BMD (Ct.BMD, mg hydroxyapatite/cm³) [21,22]. Ct.Po is calculated as the amount of void space in the cortex using Image Processing Language (IPL, Version 5.08b; Scanco Medical). Ct.Th is measured directly using a distance transform method and Ct.BMD is defined as the average BMD in the cortical bone compartment [20,21].

Individual trabeculae segmentation analyses

In addition to the standard analysis, ITS was applied to assess the orientation and the characteristics of plate and rod trabecular elements [13,23]. Briefly, this method creates a skeleton of the trabecular region and classifies each trabecular element as a surface or curve; through an iterative reconstruction method, each voxel of the original image is classified as belonging to either an individual plate or rod [13,23]. Based on the three-dimensional evaluations, plate and rod bone volume fraction (pBV/TV and rBV/TV) and plate and rod number (pTb.N and rTb.N, 1/mm) were evaluated. Plate-to-rod ratio (P-R ratio), a parameter of plate versus rod characteristics of trabecular bone, was defined as plate bone volume divided by rod bone volume. The average size of plates and rods was quantified by plate and rod thickness (pTb.Th and rTb.Th, mm), plate surface area (pTb.S, mm²), and rod length (rTb.L, mm). Intactness of the trabecular network was characterized by plate-plate, plate-rod, and rod-rod junction density (P-P, P-R, and R-R Junc.D, 1/mm³), calculated as the total junctions between trabecular plates and rods normalized by the bulk volume. Orientation of trabecular bone network was characterized by axial bone volume fraction (aBV/TV), defined as axially aligned bone volume divided by the bulk volume [13,23].

Micro finite element analyses

Each thresholded HR-pQCT whole bone image and trabecular bone compartment image of the distal radius and tibia was converted to a micro finite element (μ FE) model. Bone tissue was modeled as an isotropic, linear elastic material with a Young's modulus of 15 GPa and a Poisson's ratio of 0.3 [18]. For each model, a uniaxial compression test was performed to calculate the reaction force under a displacement equal to 1% of the bone segment height along the axial direction. Whole bone stiffness, defined as reaction force divided by the applied displacement, characterizes the mechanical competence of both the cortical and trabecular compartments and is associated with whole bone strength [18] and fracture risk [19,24,25]. Similarly, trabecular bone stiffness characterizes the mechanical competence of trabecular bone compartment [18]. All the μ FE analyses were performed using a customized element-by-element preconditioned conjugate gradient solver [26].

Statistical analysis

All statistical analyses were performed using SAS (version 9.2; SAS Institute, Cary, North Carolina, USA). Continuous data are presented as mean value $\pm$ standard standard deviation; categorical data are presented as percentage or absolute number. Means between groups were compared using Student's *t*-tests; covariate-adjusted means between groups were compared by analysis of covariance; between group differences in correlations between DXA and HR-pQCT measures were tested with analysis of variance test of homogeneity of slopes; categorical data compared by odds ratios from χ^2 , Fisher's exact, or Jonckheere–Terpstra test for trend. No adjustments were made for multiple comparisons. A *P* value <0.05 was considered statistically significant.

Results

Characteristics of the study population

Compared with controls, HIV-infected men were similar in age and BMI, but were more likely to be African–American (Table 1). Perinatally infected men were on average 1 year younger than men infected during adolescence, but were similar with regard to BMI, race/ethnicity, and CD4⁺ cell counts (data not shown). Among perinatally infected men, mean current and nadir CD4⁺ cell counts were 474 ± 161 and 191 ± 161 cells/ μ l, respectively; 13% had a history of AIDS-defining illness, and the mean duration of ART was 12 years. Among men infected during adolescence, age of sexual debut was 15 ± 3 years, mean time since HIV diagnosis was 2.5 ± 1.0 years, and mean current/nadir CD4⁺ cell counts were $533 \pm 157/299 \pm 149$ cells/ μ l; 6% had history of AIDS-defining illness and mean duration of ART was 2 years. Proportion with HIV-1 RNA levels less than 50 copies/ μ l was the same in each group (67 versus 67%, *P* = 1.0). The majority of perinatally infected men (67%) were on protease inhibitor-containing regimens, whereas the majority of men infected during adolescence (87%) were on nonnucleoside reverse transcriptase inhibitor (NNRTI)-containing regimens. Current tenofovir use was also higher in men infected during adolescence than perinatally infected men (93 versus 67%, *P* = 0.07), although this did not reach statistical significance.

Dual-energy X-ray absorptiometry and bone turnover marker results

Bone size, as assessed by CSA by DXA scans was similar among HIV-infected and HIV-uninfected men at the spine, hip, and radius. However, aBMD Z-scores were 0.4–1.2 lower in HIV-infected men at all sites (Table 1). There were no significant differences in DXA measures between the two HIV-infected groups.

High-resolution peripheral quantitative computed tomography and cortical porosity analyses

At the radius, CSA was similar between groups, but total vBMD, trabecular vBMD, and cortical and trabecular thickness were between 6 and 19% lower in HIV-infected than uninfected groups (Figs. 1 and 2). After adjusting for race/ethnicity, total and trabecular vBMD as well as cortical and trabecular thickness remained significantly lower in the HIV-infected group (Table 2). At the tibia, CSA was similar between groups, but total and

trabecular vBMD as well as trabecular and cortical thickness were 9–18% lower in the HIV-infected group, both before and after adjustment for race. In addition, trabecular number was lower, and trabecular separation and network heterogeneity were 15–21% higher in the HIV-infected group (Table 2, Fig. 2). These measures suggest that the HIV-infected men have thinner, more widely separated, and heterogeneously distributed trabeculae and thinner cortices. There were no significant differences in cortical porosity between the HIV-infected and HIV-uninfected groups. There were no statistically significant differences in HR-pQCT measures between the two HIV-infected groups.

Individual trabeculae segmentation analysis of high-resolution peripheral quantitative computed tomography images

ITS analysis of the trabecular compartment revealed key microstructural differences in HIV-infected and HIV-uninfected groups at both the radius and tibia (Fig. 3). At the radius, pBV/TV, PR ratio, pTb.N, and pTb.Th, were 31, 30, 8, and 5% lower in HIV-infected than uninfected controls, respectively, with pBV/TV and pTb.Th remaining significant ($P<0.05$) after adjustment for race/ethnicity. Similarly, at the tibia, pBV/TV, pTb.N, and pTb.Th were 24, 7, and 4% lower in HIV-infected than uninfected controls, respectively, with significant differences at the pBV/TV, pTb.N, and pTb.Th after adjustment for race/ethnicity. There were no between group differences in rod-specific measures.

The aBV/TV was significantly lower at the radius (–23%) and tibia (–20%) in HIV-infected men than uninfected controls. At the radius, P–R and P–P junction densities were –16 and –22%, respectively, lower in HIV-infected than controls [27]. At the tibia, only the plate–plate junction density was lower, by 17% in HIV-infected than uninfected men. Most parameters remained significant after adjustment for group differences in race/ethnicity (Fig. 3). Between the men infected perinatally or during adolescence, there was no consistent pattern of microstructural differences at the radius or tibia (data not shown).

Micro finite element analysis of high-resolution peripheral quantitative computed tomography images

Differences in vBMD and cortical and trabecular microstructure were associated with significant differences in mechanical properties (Fig. 3). Trabecular stiffness was 24% lower at the radius, and whole bone stiffness was 17% lower at the radius and 14% at the tibia. There were no significant differences in men infected perinatally and during adolescence (data not shown).

Discussion

HIV-infected men in their early 20s, an age when most have achieved peak bone mass, had lower aBMD by DXA at all sites measured, whether infected perinatally or during adolescence. Lower spine, hip, and forearm aBMD could not be accounted for by smaller bone size, as CSA was similar by DXA and HR-pQCT at the radius and tibia. By HR-pQCT, total vBMD was significantly lower at both radius and tibia, predominantly due to marked deficits in the trabecular compartment. Although cortical vBMD did not differ, HIV-infected men had lower cortical area and significantly thinner cortices. Trabecular microarchitecture

was markedly abnormal at the tibia and radius in HIV-infected men, both by standard HR-pQCT analyses, which showed thinner, more widely separated and heterogeneously distributed trabeculae, and by advanced imaging of individual trabeculae by ITS, which revealed fewer and thinner trabecular plates, fewer connections between plates and also between plates and rods. Importantly, these microstructural differences were reflected in lower estimated whole bone and trabecular stiffness (strength) in HIV-infected than uninfected men. The majority of these findings remained significant after adjusting for group differences in race/ethnicity. Our findings suggest that HIV infection and the effects of antiretrovirals early in life are associated with lower peak bone mass, markedly abnormal microarchitecture, and lower estimated bone strength.

In the largest BMD study of HIV-infected children to date, Pediatric AIDS Clinical Trials Group (PACTG) 1045 compared BMC and BMD by DXA in 236 perinatally HIV-infected and 143 HIV-uninfected boys and girls frequency matched by Tanner stage (1–5) and socio-demographic background [3]. In their adjusted models, they found that HIV-infected boys had significantly lower total body BMC and total body and spinal BMD at Tanner 5, lower BMC at Tanner 3–4, and similar BMC and BMD at Tanner 1–2, compared with HIV-uninfected boys. Our findings are consistent with the Tanner 5 results from PACTG 1045 and extend their work by demonstrating that lower peak bone mass observed in HIV-infected individuals is accompanied by microarchitectural abnormalities.

The differences we detected between HIV-infected and uninfected young men, between 6 and 19% lower total and trabecular vBMD, cortical and trabecular thickness, and the higher trabecular separation and network heterogeneity, are similar in magnitude to differences in HR-pQCT parameters observed in studies comparing postmenopausal women with and without low trauma fractures. Such studies report differences in total vBMD and trabecular vBMD ranging from 10 to 20% [8,9,25,28,29], along with differences in other cortical or trabecular parameters [19,30–32]. Similarly, the magnitude of differences in ITS parameters between HIV groups is comparable to those we documented between postmenopausal women with and without fragility fractures – between 5 and 30% differences in rod and plate BV/TV, P-R ratio, plate and rod TbN, plate Tb.Th and P-P, P-R, and R-R junction densities [12]. With μ FEA, bone stiffness was found to be 13–17% lower in postmenopausal women with ankle fractures compared with those with no fractures [19]. Therefore, these results suggest that men infected with HIV perinatally or during adolescence have lower bone strength and thus may be at higher risk of fracture than their peers at peak bone mass. With aging, both the cortical and trabecular deficits in these young men can be expected to progress further [33], placing them at even higher risk of fracture than uninfected men and perhaps also men infected with HIV later in life.

Notably, there were few differences in bone mass and structure between HIV-infected groups. Because men infected with HIV perinatally have had longer exposure to the HIV virus and to antiretroviral drugs, we had hypothesized that peak bone mass would be lower and HR-pQCT abnormalities more pronounced in perinatally infected men than those infected during adolescence. The perinatally infected group appeared to have smaller bone size as well as decreased cortical thickness and vBMD than the group infected during adolescence, but these differences did not reach statistical significance in this small study.

Mean CD4⁺ cell and HIV-1 RNA levels at the time of evaluation did not differ between groups nor did they correlate consistently with either aBMD or vBMD (data not shown). Tenofovir is the antiretroviral with the clearest association with bone loss both at the initiation and switch phases of treatment [34,35]. Therefore, the fact that a greater proportion of the group infected during adolescence was taking tenofovir than the perinatally infected group (93 versus 67%, $P = 0.24$) with longer duration of exposure (3.7 ± 3.2 versus 1.4 ± 0.8 years, $P = 0.05$) may partially explain why group differences were smaller than expected. In addition, there may be other unmeasured exposures among the group infected during adolescence that impact bone. A recent preexposure prophylaxis study found that a significant proportion of men who have sex with men at risk of HIV acquisition had low BMD at baseline that was associated with amphetamine and inhalant use [36]. It is also possible that bone mass acquisition may be particularly vulnerable to the impact of HIV infection and ART treatment during the skeletal growth phase of adolescence. A larger, longitudinal study is necessary to confirm these results.

To our knowledge, this is the first study to examine peak bone mass and bone microarchitecture with HR-pQCT in HIV-infected individuals. A major strength of our study is that the control group was similar in age, height, weight, and CSA of spine, hip, and radius; however, it remains possible that skeletal maturation is delayed and peak bone mass is acquired later in HIV-infected individuals.

This study also has several limitations. The sample size was small and may have limited our ability to detect differences between HIV-infected who contracted the disease at birth and those who contracted it during adolescence. Cortical area at the radius was approximately 15% lower in men infected perinatally than in adolescence; however, with our sample size, we had only 39% power to detect that difference. The sample size also limited our ability to determine the impact of exposure to tenofovir or other antiretrovirals on BMD. Additionally, we do not have data on important covariates such as vitamin D levels, diet, and exercise, which may have attenuated expected differences in BMD. Another limitation of the study is the difference in race/ethnicity between the groups. Age at which BMD acquisition reaches a plateau phase is similar across race and ethnicity, but black men attain higher mean aBMD values at the hip and spine than nonblack (Asian, Hispanic, and whites) male youth [37]. There may also be microarchitectural differences between African-Americans and Hispanics, but data are limited. Additionally, the majority of our Hispanics were of Caribbean origin. There is a great deal of racial admixture in these Hispanic populations, and aBMD and HR-pQCT characteristics of Hispanics of Caribbean origin have not been characterized. As there were more African-Americans than Hispanics in the HIV-infected group, and aBMD is likely to be greater in African-Americans than Hispanics, the race/ethnicity imbalance of our sample would have biased our findings toward the null. Finally, the differences in HR-pQCT parameters remained significant after adjustment for race/ethnicity. Finally, there are some technical limitations due to the resolution when measuring Ct.Po and performing ITS; however, these methods have been validated against higher resolution technologies [11,21].

Recent data from several large cohort studies suggest that incidence of fragility and nonfragility fractures are 1.2–2.4 times greater in HIV-infected than uninfected adults [38–

40]. Although the largest difference in fracture rates occur among older individuals [41], higher fracture rates have also been reported in younger HIV-infected individuals [39,40,42]. Our data suggest that men infected with HIV early in life have lower peak bone mass, a thinner cortical shell, markedly abnormal trabecular bone microstructure with deficiencies in trabecular plates and axial bone volume fraction, and reduced bone strength. These deficits may place them at higher risk of fractures as they age than uninfected individuals and HIV-infected individuals who were infected later in life, after acquisition of peak bone mass. With more than 3 million children under age 15 and nearly 5 million young adults, age 15–24 living with HIV worldwide [43], bone health of those infected with HIV early in life is an area of concern and warrants further study.

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Fig. 1. Representative high-resolution peripheral quantitative computed tomography (HR-pQCT) images from 24-year-old HIV-infected (left) and HIV-uninfected (right) African-American men at the radius (top) and tibia (bottom)

HR-pQCT, high-resolution peripheral quantitative computed tomography.

Fig. 2. Percentage difference in high-resolution peripheral quantitative computed tomography measures between HIV-infected and HIV-uninfected men at the radius and tibia

Ct.Th, cortical thickness; HR-pQCT, high-resolution peripheral quantitative computed tomography; Tb.N, trabecular number; Tb.Sp (SD), trabecular separation standard deviation; Tb.SP, trabecular separation; vBMD, volumetric bone mineral density. * $P < 0.05$ after adjustment for race/ethnicity.

Fig. 3. Percentage difference in individual trabeculae segmentation and micro finite element analysis measures between HIV-infected and HIV-uninfected men at the radius and tibia
 μFEA, micro finite element analysis; ITS, individual trabeculae segmentation; pBV/TV and rBV/TV, plate and rod bone volume fraction; P-P, P-R, and R-R Junc.D, plate-plate, plate-rod, and rod-rod junction density; pTb.N and rTb.N, plate and rod number; P-R ratio, plate-to-rod ratio; pTb.Th and rTb.Th, plate and rod thickness; pTb.S, plate surface area; rTb.l, mm, rod length. * $P < 0.05$ after adjustment for race/ethnicity.

Table 1
Characteristics and dual X-ray absorptiometry results of young men infected with HIV early in life and uninfected controls

	HIV-infected (N = 30)	Uninfected (N = 15)	P value
Patient characteristics			
Age	22.5 ± 0.3	22.0 ± 0.5	0.31
Race/ethnicity (African–American, Hispanic)	60% AA; 40% H	20% AA; 80% H	0.01
Height (cm)	173 ± 2	173 ± 2	0.97
Weight (kg)	77 ± 4	75 ± 5	0.72
BMI (kg/cm ²)	26.0 ± 0.6	24.8 ± 1.3	0.71
Current smoking (%)	43%	20%	0.26
Alcohol use > 2 drinks/day (%)	3%	0%	0.49
DXA cross-sectional area and body composition			
LS CSA (cm ²)	63.5 ± 1.1	64.9 ± 2.8	0.45
FN CSA (cm ²)	5.4 ± 0.1	5.2 ± 0.1	0.34
TH CSA (cm ²)	39.7 ± 0.7	40.1 ± 1.5	0.78
R13 CSA (cm ²)	3.0 ± 0.1	2.9 ± 0.1	0.41
UDR CSA (cm ²)	3.8 ± 0.9	3.8 ± 1.0	0.67
Total body fat (%)	22.3 ± 1.1	21.3 ± 1.9	0.61
Trunk fat (%)	21.3 ± 1.4	19.8 ± 2.2	0.59
DXA bone mineral content and density			
LS aBMD (g/cm ²)	1.04 ± 0.02	1.11 ± 0.03	0.049
FN aBMD (g/cm ²)	0.97 ± 0.03	1.06 ± 0.04	0.07
TH aBMD (g/cm ²)	1.07 ± 0.03	1.15 ± 0.04	0.09
R13 aBMD (g/cm ²)	0.75 ± 0.01	0.77 ± 0.02	0.01
UDR aBMD (g/cm ²)	0.50 ± 0.01	0.56 ± 0.01	0.002
LS Z-score	−1.01 ± 0.23	0.01 ± 0.27	<0.01
FN Z-score	−0.37 ± 0.19	0.50 ± 0.25	0.01
TH Z-score	−0.22 ± 0.20	0.62 ± 0.25	0.01
R13 Z-score	−1.27 ± 0.25	−0.05 ± 0.32	0.007
UDR Z-score	−0.70 ± 0.18	0.24 ± 0.21	0.002

AA, African–American; H, Hispanic; aBMD, areal bone mineral density; BMC, bone mineral content; CSA, cross-sectional area; DR, 1/3 distal radius; DXA, dual X-ray absorptiometry; FN, femoral neck; LS, lumbar spine; TH, total hip; UDR, ultradistal radius.

Table 2
High-resolution peripheral quantitative computed tomography measures in young men infected with HIV early in life and uninfected controls (mean $\pm$ SEM)

	HIV-infected (N = 30)	Uninfected (N = 15)	P value	Perinatal infection (N = 15)	Adolescent infection (N = 15)	P value
Radius						
Total area (mm ²)	344 $\pm$ 14	328 $\pm$ 23	0.32	337 $\pm$ 20	351 $\pm$ 20	0.59
Ct. area (mm ²)	63.4 $\pm$ 2.8	73.7 $\pm$ 3.3	0.03	58.7 $\pm$ 4.1	68.1 $\pm$ 3.7	0.10
Tb. area mm ²)	281 $\pm$ 14	255 $\pm$ 26	0.32	278 $\pm$ 22	283 $\pm$ 18	0.85
Total vBMD (mgHA/cm ³)	324 $\pm$ 11	388 $\pm$ 15	0.002*	318 $\pm$ 21	330 $\pm$ 10	0.61
Ct. vBMD (mgHA/cm ³)	814 $\pm$ 13	829 $\pm$ 15	0.49	796 $\pm$ 20	831 $\pm$ 15	0.17
Tb. vBMD (mg HA/cm ³)	188 $\pm$ 6	233 $\pm$ 7	>0.0001*	187 $\pm$ 9	189 $\pm$ 9	0.85
Ct. thickness (μ m)	992 $\pm$ 37	1170 $\pm$ 53	0.006*	955 $\pm$ 64	1027 $\pm$ 36	0.32
Ct. porosity (%)	6.5 $\pm$ 0.4	6.7 $\pm$ 0.5	0.77	6.7 $\pm$ 0.6	6.4 $\pm$ 0.4	0.68
Tb. thickness (μ m)	75 $\pm$ 2	88 $\pm$ 4	0.004*	72 $\pm$ 3	78 $\pm$ 4	0.22
Tb. number (1/mm)	2.0 $\pm$ 0.04	2.1 $\pm$ 0.1	0.12	2.2 $\pm$ 0.1	2.0 $\pm$ 0.1	0.19
Tb. separation (μ m)	408 $\pm$ 11	370 $\pm$ 18	0.052	396 $\pm$ 14	420 $\pm$ 16	0.27
Tb. separation SD (μ m)	166 $\pm$ 6	146 $\pm$ 10	0.10	159 $\pm$ 7	173 $\pm$ 9	0.23
Tibia						
Total area (mm ²)	811 $\pm$ 27	775 $\pm$ 45	0.22	787 $\pm$ 40	834 $\pm$ 38	0.40
Ct. area (mm ²)	149 $\pm$ 5	176 $\pm$ 9	0.007*	147 $\pm$ 8	152 $\pm$ 6	0.63
Tb. area mm ²)	661 $\pm$ 27	599 $\pm$ 45	0.22	640 $\pm$ 40	683 $\pm$ 38	0.45
Total vBMD (mgHA/cm ³)	320 $\pm$ 10	386 $\pm$ 15	0.0004*	320 $\pm$ 14	320 $\pm$ 14	0.98
Ct. vBMD (mgHA/cm ³)	876 $\pm$ 8	880 $\pm$ 11	0.79	863 $\pm$ 11	888 $\pm$ 10	0.10
Tb. vBMD(mg HA/cm ³)	186 $\pm$ 6	230 $\pm$ 10	0.0003*	187 $\pm$ 8	186 $\pm$ 9	0.93
Ct. thickness (μ m)	1483 $\pm$ 45	1803 $\pm$ 120	0.02*	1462 $\pm$ 70	1503 $\pm$ 57	0.66
Ct. porosity (%)	5.9 $\pm$ 0.3	7.4 $\pm$ 0.7	0.58	6.1 $\pm$ 0.4	5.7 $\pm$ 0.3	0.40
Tb. thickness (μ m)	80 $\pm$ 2	88 $\pm$ 9	0.052*	80 $\pm$ 3	80 $\pm$ 4	0.95
Tb. number (1/mm)	2.0 $\pm$ 0.1	2.2 $\pm$ 0.1	0.02	2.0 $\pm$ 0.1	2.0 $\pm$ 0.1	0.82
Tb. separation (μ m)	438 $\pm$ 13	380 $\pm$ 24	0.02*	434 $\pm$ 16	442 $\pm$ 21	0.77
Tb. separation SD (μ m)	202 $\pm$ 9	166 $\pm$ 14	0.03*	198 $\pm$ 10	206 $\pm$ 16	0.69

Ct, cortical;HR-pQCT, high-resolution peripheral quantitative computed tomography;Tb, trabecular;vBMD, volumetric bone mineral density. Ct. thickness, vBMD, and porosity were calculated using the autosegmentation method described in methods.

* $P < 0.05$ after adjustment for race/ethnicity.