Poster #774

Predictors of longitudinal change in bone mineral density in a cohort of HIV-positive and negative subjects

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Background

Low bone mineral density (BMD) and osteoporosis have emerged as significant causes of morbidity in the long-term management of HIV.

Although BMD loss is consistently observed with antiretroviral therapy (ART) initiation, it is unclear if ongoing changes in BMD differ between those with and without HIV.

Objective

- To compare rates of change in BMD over time between HIV-positive (HIV+) and HIV-negative (HIV-) subjects.
- To determine HIV-related predictors of change in BMD over time.

Methods

Understanding the Pathology of Bone Disease in HIV-infected subjects (HIV UPBEAT) is a 3-year, observational cohort study that enrolled HIV+ subjects from the Mater Misericordiae University Hospital and HIV- subjects recruited from the greater Dublin general population.

Dual-energy X-ray absorptiometry at femoral neck (FN), total hip (TH) and lumbar spine (LS) were performed at study entry and annually for 3 years.

Demographic, clinical, medication data and fasting bloods were collected, including bone turnover markers (C-terminal cross-linking telopeptide of type-1 collagen (CTX-1), procollagen type-1 amino-terminal propeptide (P1NP), and osteocalcin (OC).

Longitudinal mixed models were used to compare and determine predictors of absolute BMD and rate of absolute change in BMD in the whole cohort and within the HIV+ group. Data is presented as median (IQR) unless otherwise stated.

Results

474 enrolled subjects (210 HIV+) completed the baseline study visit with results previously reported [1]. Follow-up analyses included 384 subjects (of whom 176 were HIV+) with at least two follow-up BMD measurements. Of the 384 subjects, 120 subjects (of whom 57 were HIV+) contributed 2 and 264 subjects (of whom 119 were HIV+) contributed 3 BMD annual measurements.

Subjects were followed up for 103 (88-177) weeks. Compared to HIV- subjects, those with HIV were younger, more likely to be male, current smokers and less likely to be Caucasian (Table 1).

In the HIV+ group, HIV acquisition risk groups were 51% heterosexual contact, 31% men who have sex with man (MSM) and 17% injecting drug users. Time from HIV diagnosis was 4.0 (2.0-9.0) years.

The majority of subjects (88%) were on ART, 73% were currently on tenofovir (TDF)-containing ART and 41% on protease inhibitor (PI)-containing ART.

The median (IQR) total ART exposure, exposure to TDF and exposure to PI were 2.9 (0.7-5.4) years, 1.3 (0.1-2.9) years, and 0.3 (0.0-2.6) years respectively.

Results

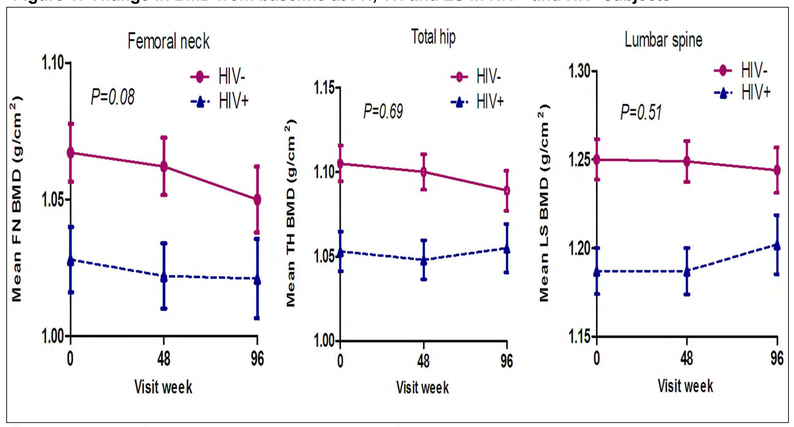
Table 1: Characteristics of HIV-positive and HIV-negative subjects

	HIV+ (n=176)	HIV- (n=208)	*P*
Age	39 (34-46)	43 (35-50)	0.04
Male *	107 (61%)	95 (46%)	0.003
Caucasian *	108 (61%)	171 (82%)	<0.001
Current smoker *	60 (34%)	31 (15%)	<0.001
BMI (kg/m^2)	26 (23-30)	27 (24-30)	0.07
25 (OH) Vit D (mmol/L)	50.5 (31.0-70.5)	53.0 (37.0-75.0)	0.33
FN BMD–BL (g/cm^2)	1.024 (0.927-1.135)	1.055 (0.964-1.159)	0.003
TH BMD-BL (g/cm^2)	1.061 (0.942-1.157)	1.107 (1.000-1.196)	0.003
LS BMD-BL (g/cm^2)	1.164 (1.061-1.304)	1.238 (1.135-1.348)	0.001

* n(%); BMI, body mass index, BL-baseline

Compared to the HIV- group, the HIV+ group had significantly lower baseline absolute BMD (Table 1).

Figure 1: Change in BMD from baseline at FN, TH and LS in HIV+ and HIV- subjects



P-values were obtained from the time*group interactions in the mixed effects model

Absolute change in BMD

Overall in the cohort, BMD significantly declined at FN (0.43% per year; p<0.001), TH (0.41% per year; p<0.001) and LS (0.28% per year; p=0.014). In the HIV+ group, BMD significantly declined at FN (0.6% per year; p=0.001), TH (0.44% per year; p<0.001) and not LS (0.22% per year; p=0.22). Similarly BMD significantly decline at FN (0.27% per year; p=0.025), TH (0.35% per year; p<0.001) and not LS (0.34% per year; p=0.08) in the HIV- group.

There were no significant between-group difference in rate of absolute change in BMD (Figure 1): FN (-0.004 g/cm^2/year, p=0.08), TH (-0.001 g/cm^2/year, p=0.69), LS (+0.002 g/cm^2/year, p=0.51); Further adjustment for age, gender, ethnicity, smoking status and body mass index in the mixed effects model did not alter the conclusion.

Results

HIV-specific analysis

In the unadjusted mixed effects regression analysis, having started ART less than 3 months prior to or during study follow-up was associated with a greater decline in BMD at all 3 sites. Higher baseline P1NP was associated with a reduced decline in BMD at all 3 sites.

Higher baseline PTH was associated with a reduced decline in BMD at FN and TH but not LS. Higher baseline CTX, OC and current PI use were associated with a reduced decline in BMD only at FN. Being a current smoker was associated with a greater decline in BMD only a TH.

Table 2: Multivariable mixed effects models for predictors of absolute change in BMD at FN, TH and LS in HIV+ subjects

	FN BMD*			TH BMD‡			LS BMD†		
	Effect on FN slope (g/cm^2/yr)	95% CI	*P*	Effect on TH slope (g/cm^2/yr)	95% CI	*P*	Effect on LS slope (g/cm^2/yr)	95% CI	*P*
Age >30 vs <30 years	-0.013	-0.02; -0.002	0.02	-	-	-	-	-	-
Caucasian vs non-Caucasian ethnicity	-0.011	-0.02; -0.003	0.006	-	-	-	-	-	-
PTH (per 1 pmmol/L)	0.0017	0.0005; 0.003	0.007	0.0006	-0.0002; 0.001	0.12	-	-	-
ART < 3months prior/during study vs continuous follow-up ART	-0.016	-0.026; -0.006	0.002	-0.014	-0.02; -0.007	<0.001	-0.025	-0.04; -0.01	<0.001
Not on ART vs continuous ART	-0.019	-0.03; -0.004	0.01	-0.0024	-0.01; 0.008	0.65	-0.0062	-0.024; 0.01	0.48

*Model adjusted for gender, education level, BMI, baseline ALP, 25(OH)D and CTX, ‡model adjusted for gender, ethnicity, BMI, baseline ALP, PTH and CTX
†model adjusted for ethnicity, BMI, baseline ALP, and CTX

In multivariable mixed effects models, having started ART less than 3 months prior to or during study follow-up remained independently associated with a greater decline in BMD at all 3 anatomical sites (Table 2).

Age above 30 years and Caucasian ethnicity, and not being on ART during study follow-up were independently associated with greater decline in BMD over time but only at FN, while higher baseline PTH was independently associated with a reduced decline in BMD at FN (Table 2).

We found no association between change in BMD and current or cumulative exposure to TDF, PI or other HIV-associated factors such as CD4+ T-cell count, or traditional risk factors for low BMD such as gender, current smoking, 25-hydroxy-vitamin D and BMI .

Conclusion

BMD decreased over time at FN, TH and LS in the whole cohort and only at FN and TH within groups. There were no differences in the rate of BMD decline between the HIV+ and HIV- groups.

Greater BMD decline was observed in subjects recently started on ART, aged above 30 years and in Caucasians. Less decline in BMD was observed with higher baseline PTH.

There was no evidence of greater BMD decline in those on established ART or with exposure to specific ART drugs such as TDF or PI.

Further research is required to determine if these findings are consistent beyond 3-years of follow-up.

References

[1] Cotter AG, Sabin CA, Simelane S, Macken A, Kavanagh E, Brady JJ, et al. Relative contribution of HIV infection, demographics and body mass index to bone mineral density. AIDS. 2014 Sep 10;28(14):2051-60

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