HAART is Associated With Reduced Risk of Osteoporosis-Related Fractures

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Background

- People living with HIV (PLWH) face a higher risk of osteoporosis-related fractures (ORF) compared with HIV-negative individuals.
- HIV-related systemic inflammation and antiretroviral therapy (ART), particularly tenofovir disoproxil fumarate (TDF), have been associated with reduced bone mineral density; but the association between ORF and these factors is not as clearly described .
- In this study we investigated the association of HIV-related factors including viral suppression and ART exposure with the risk of ORF among PLWH in British Columbia, Canada (BC).

Materials and Methods

- Data from the Comparative Outcomes and Service Utilization Trends (COAST) study was utilized for this study. COAST is a population-based cohort study examining health outcomes and health services use of all known PLWH ≥ 19 years of age in BC and a 10% sample of the BC general population ≥ 19 years of age. HIV positive individuals who had initiated ART at ≥ 19 years of age and were ART naïve at study baseline were included in this analysis. All individuals with unknown sex were excluded.
- Outpatient physician and hospital-based administrative claims data from 1996-2013 were examined for diagnoses of ORF using International Classification of Disease (ICD) 9/10 code algorithms based on published case definitions. This analysis defined ORFs as humerus, vertebrae, and hip fractures[1].
- The effect of sex, age at ART initiation, previous injuries, history of injection drug use (IDU), ART initiation era and viral load (VL) <500 copies/ml on the risk of ORF was assessed by logistic generalized estimating equation model.
- Age and sex adjusted incidence rates were calculated using the 2011 Canada population as reference.

Table 1. Multivariate Model

Variable	Odds Ratio	95% CI	
Sex			
Male [ref]	1.00		
Female	1.46	1.11	1.93
IDU			
No [ref]	1.00		
Yes	2.08	1.58	2.73
Age at ART initiation (per 10 years increase)	1.53	1.36	1.72
Any injuries except falls before ORF*			
No [ref]	1.00		
Yes	3.88	2.99	5.03
ART initiation era			
<=1999 [ref]	1.00		
2000-2003	0.78	0.59	1.04
2004-2007	0.53	0.39	0.72
>=2008	0.20	0.14	0.30
Proportion of VL<500 copies/ml until ORF (10%)	0.96	0.93	1.00

Table 2. Univariate Model

Variable	Odds Ratio	95%CI	
Length of time on ART until ORF (1 year)*	0.92	0.89	0.94
Length of time on NRTI (except TDF) until ORF (1 year)*	0.89	0.86	0.92
Length of time on NNRTI until ORF (1 year)*	0.92	0.88	0.96
Length of time on PI until ORF (1 year)*	0.96	0.93	0.99
Length of time on TDF until ORF (1 year)*	0.85	0.79	0.92

Note: Only fractures occurring among PLWH after ART initiation were included. For TDF, only people who initiated ART after 01 December 2001 were considered.

CI: Confidence Interval. IDU: Intravenous Drug Use. ART: Antiretroviral Therapy. ORF: Osteoporosis-related Fracture. VL: plasma HIV-1 RNA viral load. TDF: tenofovir disoproxil fumarate. NRTI: Nucleoside / Nucleotide Reverse Transcriptase Inhibitors. PI: Protease Inhibitors. Injuries include motor vehicle collision, land transportation injuries, self harm and assault. * Are time-varying variables.

Results

- A total of 6,846 PLWH and 514,619 HIV negative individuals were included in the incidence analysis.
- ORF occurred in 416 PLWH and 28,028 HIV negative individuals (6.08% vs. 5.45% p=0.02).
- Among PLWH, 63% of the first ORF occurred before the age of 50 years of age, vs. 34% in the HIV negative group (p<.0001).
- In a multivariate analysis, female sex, older age at ART initiation, IDU and previous injuries were associated with increased odds of ORF. Later ART initiation era and higher proportion of time with VL <500 copies/ml were associated with reduced odds of ORF (Table 1).
- ART drug classes and TDF were negatively associated with ORF. (Table2)

Conclusions

- Higher rates of ORF were found in PLWH vs. HIV negative individuals and among PLWH, a higher proportion of ORFs occurred before the age of 50.
- In PLWH, having a lower VL and longer length of time on ART were associated with reduced odds of ORF, regardless of ART regime.
- We were unable to show an association between ORF and TDF exposure.
- Early initiation of ART and sustained VL <500 copies/ml may reduce the odds of ORF in PLWH.

References

1. Lix LM, Azimaee M, Osman BA, Caetano P, Morin S, Metge C, et al. Osteoporosis-related fracture case definitions for population-based administrative data. BMC Public Health. 2012 May 18;12:301.

Funding. COAST is funded by the Canadian Institutes of Health Research, through an Operating Grant (#130419) and a Foundation Award to RSH (#143342). Additional support provided by the BC Centre for Excellence in HIV/AIDS.