16th Conference on Retroviruses and Opportunistic Infections, Montreal, QC, February 2009

Preferential Bone Demineralization at the Hip in Treated HIV(+) Males: Another Example of Premature Aging in HIV Disease?

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Abstract

Background: Bone demineralization occurs more frequently in HIV (+) pts than in HIV(-) controls. We evaluated bone mineral density (BMD) at the lumbosacral (LS) spine and total hip (TH) regions in a cohort of HIV(+) males, and compared the extent of bone loss to that in HIV(-) subjects at risk of bone demineralization.

Methods: DXA scans performed on stable, treated HIV(+) males were reviewed to determine LS & TH T-scores and prevalence of BMD loss. These results were compared to DXA's available from historical controls consisting of unselected, HIV(-) males referred for BMD evaluation. Controls were age matched 1:1 to cases. Cases and controls were categorized as ≤50 y.o. or >50 y.o. to evaluate age-related effects. Median (95%±CI) T-scores were compared by the Mann-Whitney U test. Differences between anatomic site-related prevalences of normal WHO-determined BMD were compared by the Chi-square test.

Results: DXA scans on 127 treated HIV(+) males (median age 47 [46,49], range 29-77, median CD4's 435 [357,480], 65% with VL <50), were compared to 127 HIV(-) males. T-scores at the LS & TH in cases and controls, both ≤50 & >50 y.o. are presented in the Table. The T-score at the TH in younger HIV(+) pts was lower than in younger HIV(-) pts (-1.8[-2.0,-1.3] vs -1.0[-1.4,-0.8], p=0.0000). At the TH there were fewer younger HIV(+) vs HIV(-) pts with normal BMD (26% vs 53%, p=0.0007). The prevalence of normal BMD at the TH was less in younger HIV(+) than in older HIV(-) pts (26% vs 55%, p=0.03). The prevalence of normal BMD at the LS was similar in HIV(-) vs HIV(+) pts regardless of age.

Conclusion: In both younger and older treated HIV(+) males, more BMD loss occurs at the TH than at the LS spine. This differs from the pattern of BMD loss observed in age-matched controls wherein the BMD is similar at the TH and the LS in both younger and older subjects. Significantly, the extent of BMD loss at the hip in younger HIV(+) males is greater than in older controls. This preferential loss of hip BMD, occurring much earlier in this population, may predict an increased risk of morbidity and fragility fractures.

	HIV(-) n=127		HIV(+) n=127	
Age	43 (42,45)	56 (53,58)	43 (41,45)	56 (54,58)
N	80	47	77	50
LS T-score	-1.7[a] (-2.23, -1.3)	-1.9[b](-2.4, -1.5)	-1.1[c](-1.3, -0.9)	-1.2 (-1.53, -1.0)
TH T-score	-1.0[a,d] (-1.4, -0.8)	-1.2[b] (-1.7, -0.8)	-1.8[c,d] (-2.0, -1.3)	-1.5 (-2.1, -1.1)
Medians with the same letters are significantly different from each other				

RESULTS I: Demographics + Subgroup Characteristics

Group	N	Median Age	CD4	HIV VL<50
HIV(+)	127	47 (46.49)	435 (357, 480)	68%
• >50 yr.	52	56 (54,58)	438 (323, 513)	67%
• ≤49 yr.	75	43 (41,45)	429 (323, 493)	66%
HIV(-)	127	48 (46,50)	-	-
• >50 yr.	51	56 (53,58)	-	-
• ≤49 yr.	76	43 (41,45)	-	-

INTRODUCTION (I)

- Treated HIV(+) persons who are living longer may be at increased risk of developing serious non-HIV complications similar to the aging general population[1]
- In older HIV(-) persons, bone demineralization occurs frequently contributing to significant morbidity and mortality
- Bone demineralization is more common in treated HIV(+) subjects than in HIV(-) controls[2,3]

BONE MINERAL DENSITY DEFINITIONS (WHO)*

Status	T-score
Normal BMD	> -1.0
Osteopenia	-1.0 and -2.5
Osteoporosis	< -2.5
T-score indicate the number of SD's below (a) young normal controls	

* Assessment of fracture risk and its application to screening forpost-menopausal osteoporosis. WHO technical report seriies 843. Geneva: WHO, 1994:1-129
N.B. Derived and validated only for postmenopausal women

RESULTS II: ARV history at time of DXA scan

ARV	Prevalence of use	Median exposure (m)/patient
PI-HAART	64%	-
NNRTI-HAART	33%	-
AZT	34%	49
D4T	40%	43
3TC	88%	50
DDI	15%	28
TDF	13%	16
ABC	39%	23
NVP	11%	25
EFV	22%	22
KLT	24%	55
SQV	53%	30
IDV	56%	33
ATV	5%	20
NLF	28%	17

RESULTS V: 10 Year Fracture Risk for Men

At-risk Controls (n-52				
Low (10%)	LS -	44%	Low (10%)	LS - 31%
	FN -	17%		FN - 50%
	TH -	2%		TH - 2%
Moderate (10-20%)	LS -	12%	Moderate (10-20%)	FN - 10%
	FN -	6%		TH - 8%
High (<20%)	LS -	2%	High (<20%)	FN - 2%

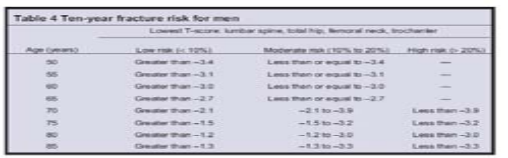


Table 4 Ten-year fracture risk for men

Siminoski K et al. JACR 2005;56(3):178-88

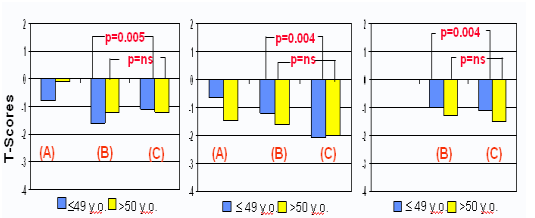
INTRODUCTION (II)

- Treated HIV(+) males may have higher fracture rates than HIV(-) controls[4,5]
- The 10 year risk of bone fractures in HIV(-) persons can be predicted using the age-adjusted BMD T-score[6]
- The extent of bone demineralization and fracture risk profile of treated HIV(+) persons is unknown

METHODS (I)

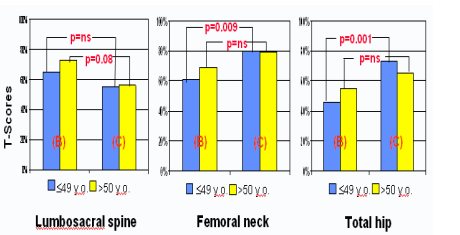
- DXA scans routinely obtained on treated HIV(+) males were reviewed and T-scores at the lumbosacral spine (LS), femoral neck (FN) and total hip (TH) regions were determined
- Similar data was determined in a group of age-matched uninfected subjects referred for DXA scanning because of clinical suspicion of osteoporosis
- Data on regional T-scores on control patients from a general population survey[7] were obtained for comparison with the other two cohorts

RESULTS III: Regional T-scores in distinct age-matched cohorts



A – CaMos (control Canadian males[5])
B – MUHC ("at risk" HIV negative)
C – IDTC (HIV positive)

RESULTS IV: Prevalence of decreased bone mineral density (osteopenia + osteoporosis) in distinct age-matched cohorts



B – MUHC ("at risk" HIV negative)
C – IDTC (HIV positive)

SUMMARY:

- BMD is less at the hip region in younger HIV(+) males than in age-matched uninfected males at increased risk for osteoporosis
- BMD at the hip region in HIV(+) males younger than 50 is similar to that in HIV(-) males nearly 15 yrs older
- BMD at the lumbo-sacral spine is greater in younger HIV(+) males than in age-matched controls but in older HIV(-) males it is similar to that in older HIV(+) males
- Fewer younger than 50 yr-old HIV(+) vs HIV(-) males have normal BMD at the hip region
- Although the predicted 10-year fracture risk (at any site) remains low (<10%) in HIV(+) males greater than 50 yrs-old, it is possible that over time more hip fractures than vertebral fractures will occur, with potentially more serious long-term sequelae

HYPOTHESIS

- Bone demineralization occurs more frequently in treated HIV(+) males than in either HIV(-) males in the general population or in uninfected males at increased risk for osteoporosis
- The extent of BMD loss at distinct bone sites is significantly greater in HIV(+) males than in HIV(-) age-matched males at increased risk for bone demineralization

METHODS (II)

- Cases and the two control cohorts were grouped into those ≤49 years old and >50 years old for comparison of regional T-scores stratified by age
- Median (±95% CI) T-scores were compared by the Mann-Whitney U-test
- Differences between anatomic site-specific prevalences of non-normal BMD were compared between HIV(+) subjects and HIV(-) at-risk subjects by the Chi-Square test

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