

# COMPARATIVE ANALYSIS OF HIV+ AND HIV- INTERACTION WITH TESTOSTERONE ON BONE MINERAL DENSITY

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## ABSTRACT

**Background:** Given an increasingly younger HIV population with osteopenia/osteoporosis a retrospective controlled study was conducted to investigate the effects of testosterone on bone mineral density (BMD) in HIV infected and HIV non-infected populations.

**Methods:** A chart review was done on a group of 80 male HIV patients and 154 male control patients. The following variables were obtained from the HIV group: age, race, employment status, smoking, body mass index (BMI), duration of HIV, CD4 levels, viral load, type of antiretroviral use, co-morbidities, use of prednisone, heroin, alcohol, methadone use, ever use of androgen, bisphosphonate use, calcium use, alpha reductase inhibitor use, phosphodiesterase inhibitor use, lipids, and biochemical markers. The same variables were obtained from the control group except those pertaining to HIV and employment status. T-scores were used in both HIV and control groups to evaluate BMD.

**Results:** A univariate analysis of variance was used controlling for the following factors: age, race, BMI, prednisone, heroin, alcohol, smoking, methadone, androgen use, alpha reductase inhibitor use, phosphodiesterase inhibitor use, bisphosphonate use, and calcium use.

	free Testosterone (pg/ml)	HIV	Control	p value
Femoral neck	< 35	-1.94	-1.35	0.29
	>35	-0.65	-1.59	0.001
Lumbar spine	<35	-1.70	-0.03	0.048
	>35	-0.78	-0.52	0.52
Hip	<35	-1.10	-0.90	0.76
	>35	-0.18	-1.27	0.0005

**Conclusions:** A normal testosterone level was protective of bone mineral density in HIV-infected patients compared to the control population. At the L-spine, HIV patients with low testosterone had a lower bone mineral density ( $p < 0.05$ ). Treatment of osteopenia/osteoporosis with testosterone in HIV patients needs further evaluation.

## BACKGROUND

• Prevalence of osteoporosis in HIV-uninfected hypogonadal men is reported to be 12.3% vs. 6.0% in men with normal testosterone levels<sup>1</sup>.

• Among patients enrolled in the Study to Understand the Natural History of HIV and AIDS (SUN), 52% had osteopenia and 10% had osteoporosis. Among these patients 78% were men, 25% were black, and 80% of patients received antiretrovirals (ART)<sup>2</sup>.

• Up to 70% of treatment-naive HIV-infected men are reported to have low free testosterone<sup>3</sup>.

• Whether an isolated HIV-related hypogonadism interaction plays a role in developing osteopenia/osteoporosis is unknown.

• It remains unclear how HIV itself or other known attributable factors (such as age, sex, race, duration of HIV, ART, hypogonadism, etc.) lead to the development of osteopenia/osteoporosis.

• There is a renewed interest in the pathogenesis, diagnosis, and management of osteoporosis in this population.

## HYPOTHESIS

We hypothesize that patients with HIV with low free testosterone levels have lower T-scores.

## METHODS /STATISTICAL ANALYSIS

• A retrospective chart review was performed on two groups: 80 HIV-infected men and 154 HIV-uninfected men (see Table 1 for epidemiologic characteristics in each population).

• HIV-specific information was obtained in those men who were HIV-infected with low and normal testosterone (see Table 2).

• An analysis of covariance was done controlling for the following factors: age, race, BMI, smoking, and use of prednisone, heroin, cocaine, alcohol, methadone, androgen, alpha reductase inhibitor, phosphodiesterase inhibitor, bisphosphonate, and calcium (see Figs 1 – 3, Table 4).

• The serum free testosterone (FT) levels were measured by Quest diagnostics (using dialysis method Wood Dale II). The normal FT ranges 35 – 210 pg/mL (see Fig 4 for free vs. total testosterone correlations in HIV-infected and HIV-uninfected patients).

## TABLE 1

Patient characteristics among HIV-infected and HIV-uninfected patients with low and normal free testosterone levels

Characteristic – n(%)	HIV-infected		HIV-uninfected	
	Free Testosterone (pg/ml) < 35	> 35	< 35	> 35
Number of patients	21	59	64	90
Mean T score				
Femoral Neck	-1.94	-0.65	-1.35	-1.59
Lumbar Spine	-1.7	-0.78	-0.03	-0.52
Hip	-1.1	-0.18	-0.9	-1.27
Age (mean in years)	57	52	73	71
Ethnicity				
Black	13 (62)	24 (41)	11 (18)	18 (20)
White	7 (33)	32 (54)	51 (82)	71 (80)
Other	1 (5)	3 (5)	none	none
BMI				
underweight (<18.5 kg/m <sup>2</sup> )	2 (10)	2 (3)	2 (3)	3 (3)
normal + overweight (>18.5 kg/m <sup>2</sup> )	19 (90)	56 (97)	62 (97)	86 (97)
HTN	6 (29)	13 (22)	49 (77)	62 (69)
DM2	4 (19)	8 (14)	20 (31)	22 (24)
Hepatitis B alone	6 (29)	15 (25)	none	none
Hepatitis C alone	4 (19)	7 (12)	3 (5)	3 (3)
Hepatitis B + Hepatitis C	6 (29)	10 (17)	1 (2)	1 (1)
Heroin use	4 (20)	6 (10)	2 (3)	1 (1)
Cocaine use	5 (24)	10 (17)	0	2 (2)
Alcohol use	2 (10)	5 (9)	3 (5)	6 (7)
Smoking				
Never	4 (19)	20 (34)	23 (37)	14 (16)
Former	5 (24)	11 (19)	23 (37)	38 (44)
Current	12 (57)	28 (48)	17 (27)	35 (40)
Chronic prednisone use	none	2 (3)	6 (9)	14 (15)
Activity level				
Low (sedentary)	21 (100)	46 (78)	n/a	n/a
Moderate (neither low or high)	none	11 (18)	n/a	n/a
High (active exercise routine)	none	2 (4)	n/a	n/a
Current androgen use	7 (33)	16 (27)	15 (23)	13 (14)
Ever androgen use	11 (52)	32 (54)	20 (31)	17 (18)
Methadone use	4 (19)	3 (5)	8 (12)	1 (1)
5 alpha-reductase inhibitor use	1 (5)	2 (3)	9 (14)	17 (19)
Bisphosphonate/ Calcium use	5 (24)	16 (27)	50 (78)	61 (68)
<b>Mean biochemical markers [ref range]</b>				
Calcium (mg/dL) [8.5 - 10.1]	9.1	9	9	10.1
Albumin (g/dL) [3.5 - 5.0]	3.4	3.7	3.4	3.7
Creatinine (mg/dL) [0.8 - 1.3]	1.1	1.1	1.3	1.1
Phosphorus (mg/dL) [2.5 - 4.9]	3.1	3.9	3.4	3.1
Alkaline Phosphatase (U/L) [50 - 136]	110	103	101	99
<b>Lipids</b>				
Triglycerides (mg/dL) [0 - 149]	219	171	125	123
Total Cholesterol (mg/dL) [0 - 200]	174	171	152	161
HDL (mg/dL) [low: 40]	38	40	42	45
LDL (mg/dL) [0 - 129]	86	101	85	92

n/a - not available

## TABLE 2

HIV related characteristics in patients with low and normal testosterone

Characteristic n(%)	< 35	>35
Free testosterone (pg/ml)	21	59
Number of patients	3 (14)	19 (32)
Employed		
Duration of HIV		
< 5 years	1 (4)	6 (10)
5 - 10 years	2 (10)	21 (36)
>10 years	18 (86)	31 (54)
CD4 count		
1 - 50	none	6 (10)
100 - 350	13 (62)	19 (32)
350 - 500	3 (14)	15 (25)
>500	5 (24)	18 (31)
Viral load		
undetectable	8 (38)	29 (49)
1 - 1,000	8 (38)	22 (37)
1,000 - 10,000	4 (19)	3 (3)
10,000 - 100,000	none	none
>100,000	1 (5)	4 (4)
Ever antiretroviral use	20 (95)	57 (97)
Ever Nucleoside inhibitor use	20 (95)	58 (98)
Ever Non-nucleoside inhibitor use	14 (67)	50 (85)
Protease inhibitor use	14 (67)	30 (51)
Fusion inhibitor use	2 (10)	2 (3)

## TABLE 3

T- scores of HIV-infected and HIV-uninfected patients in Normal, Osteopenic, and Osteoporotic Range

	Normal n(%)	Osteopenia n(%)	Osteoporosis n(%)
Femoral Neck			
HIV-infected	45(57)	31(40)	2(3)
HIV-uninfected	32(21)	40(52)	42(27)
Lumbar Spine			
HIV-infected	38(47)	35(44)	7(9)
HIV-uninfected	97(62)	40(26)	18(12)
Hip			
HIV-infected	57(72)	18(23)	4(5)
HIV-uninfected	57(38)	70(47)	23(15)

## TABLE 4

T scores in HIV-infected and HIV-uninfected patients with low and normal free testosterone levels

	T scores of HIV and non-HIV patients					
	Free Testosterone (pg/ml)	HIV	Control	p value <sup>1</sup>	p value <sup>2</sup>	p value <sup>3</sup>
Femoral neck	< 35	-1.94	-1.35	0.29	0.03	0.34
	>35	-0.65	-1.59	0.001		
Lumbar spine	<35	-1.70	-0.03	0.048	0.22	0.08
	>35	-0.78	-0.52	0.52		
Hip	<35	-1.10	-0.90	0.76	0.09	0.16
	>35	-0.18	-1.27	0.005		

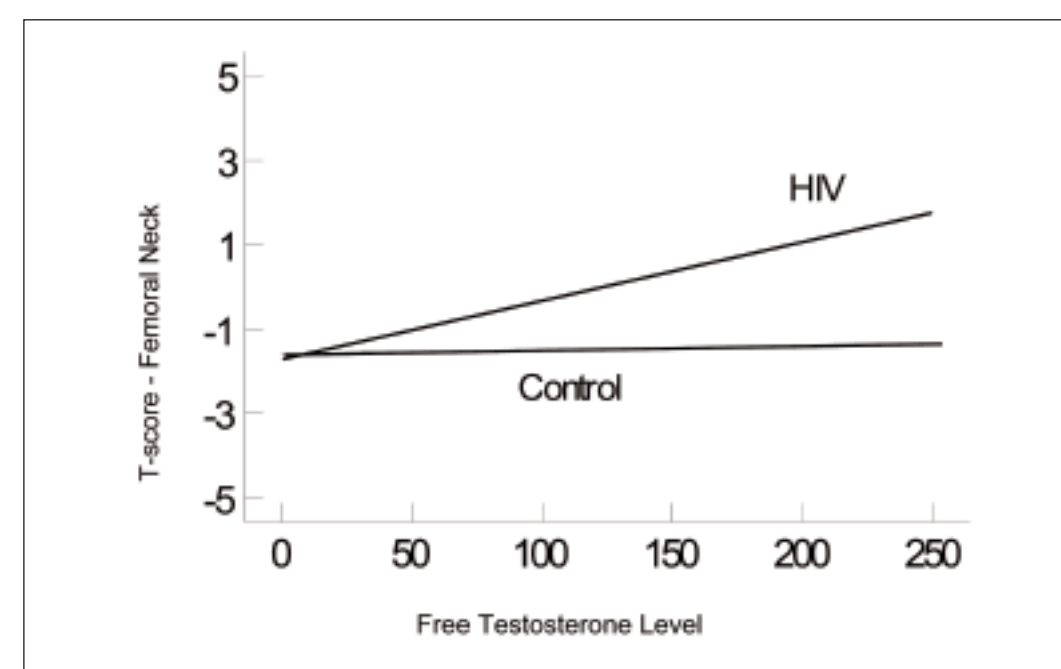
<sup>1</sup> P value describes difference between HIV and control groups

<sup>2</sup> P value describes difference between low and high testosterone levels within the HIV-infected group

<sup>3</sup> P value describes difference between low and high testosterone levels within the HIV-uninfected group

## FIGURE 1

Correlation of free testosterone levels and femoral neck BMD in HIV-infected and HIV-uninfected patients



## FIGURE 2

Correlation of free testosterone levels and lumbar spine BMD in HIV-infected and HIV-uninfected patients

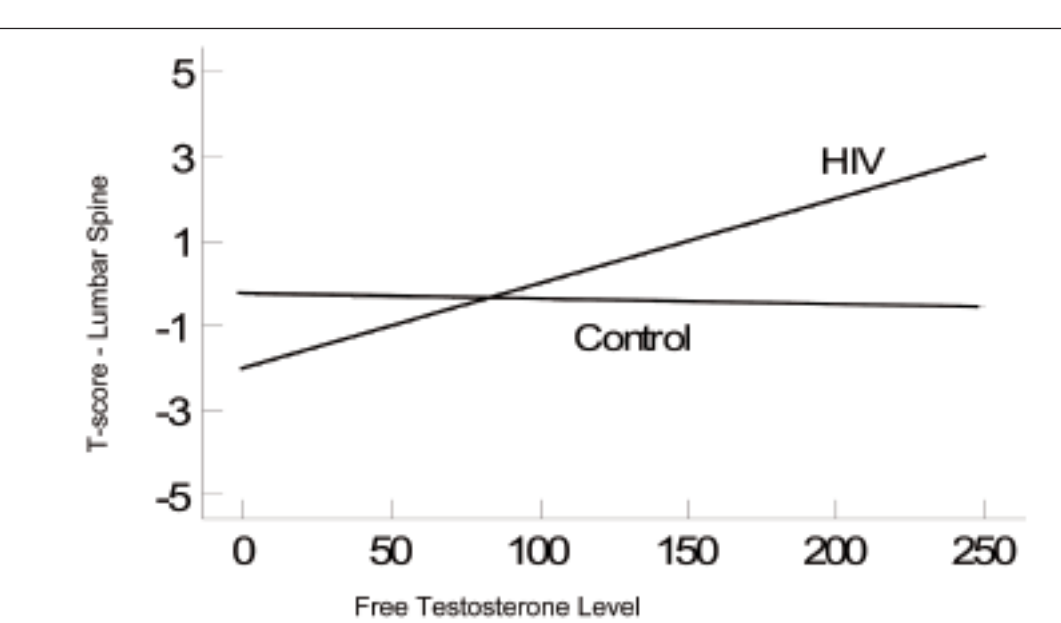


Figure 2 - Correlation of free testosterone levels and lumbar spine BMD in HIV-infected and HIV-uninfected patients

## FIGURE 3

Correlation of free testosterone levels and hip BMD in HIV-infected and HIV-uninfected patients

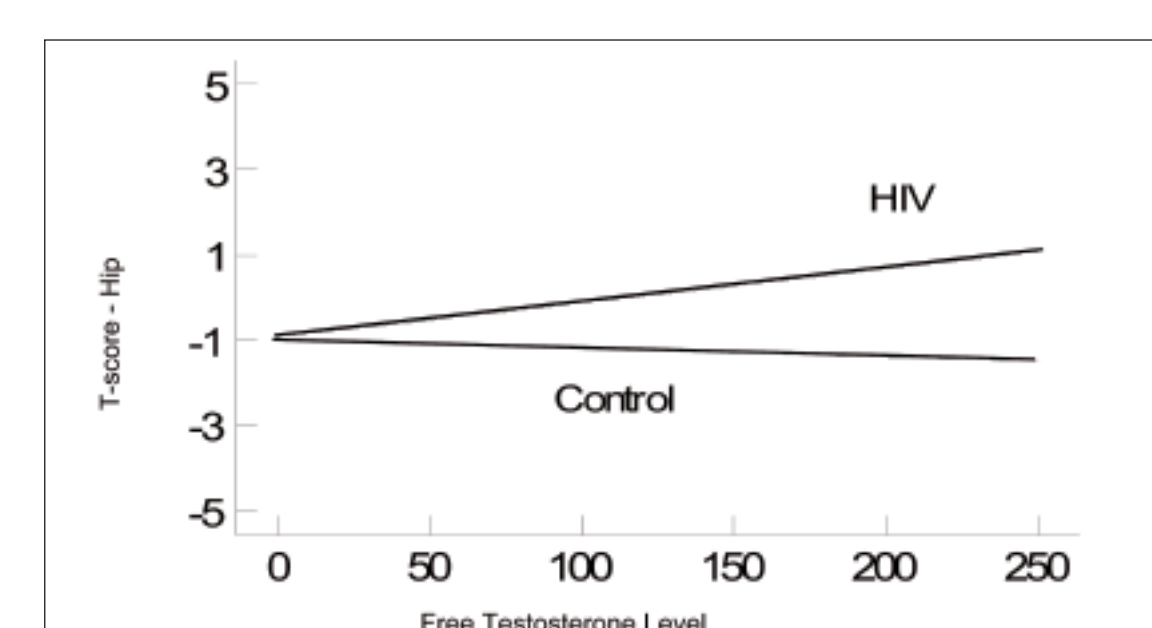


Figure 3 - Correlation of free testosterone levels and hip BMD in HIV-infected and HIV-uninfected patients

## FIGURE 4

Free and total testosterone correlation in HIV-uninfected and HIV-infected patients

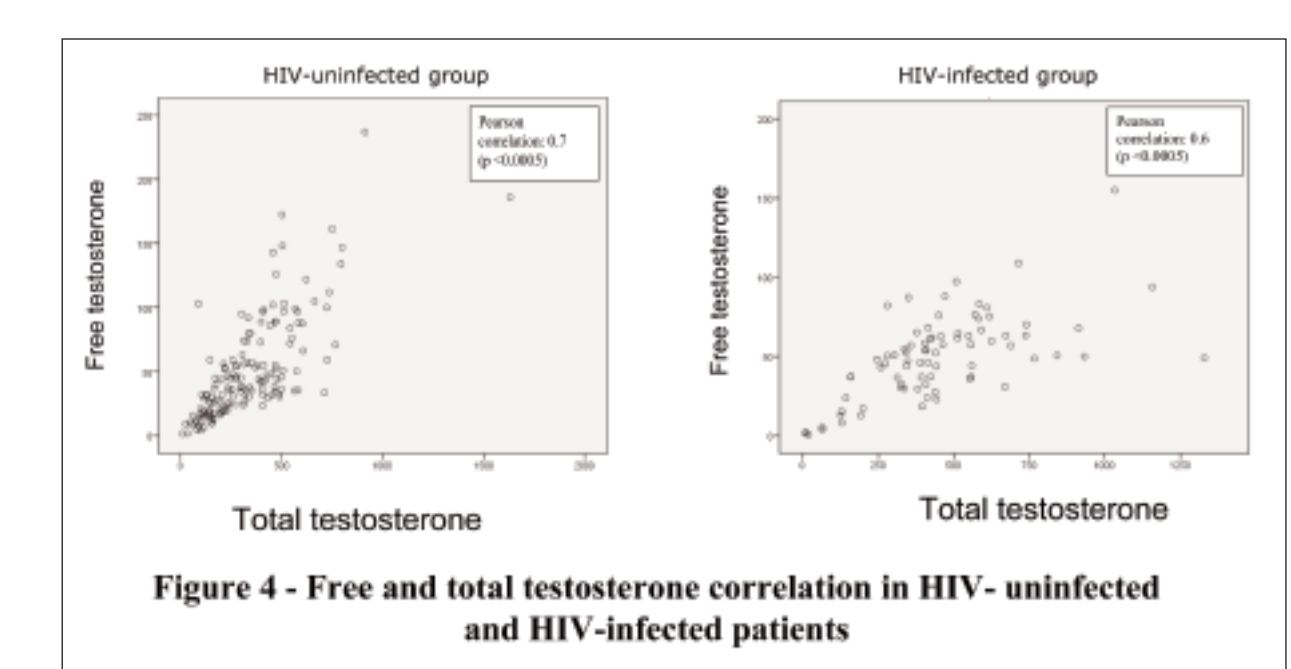


Figure 4 - Free and total testosterone correlation in HIV-uninfected and HIV-infected patients

## CONCLUSIONS

- In age-matched HIV-infected men, a lower free testosterone corresponds significantly to a lower T-score at the lumbar spine.
- A normal free testosterone level was protective of bone mineral density in HIV-infected patients compared to the control population.
- Among HIV-uninfected men, an increase in free testosterone level does not correspond to an increase in T-scores.
- Further studies evaluating the interaction of low free testosterone and HIV infection need to be conducted to better understand the bone-related effects.

## REFERENCES

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3. Wunder D.M., Bersinger N.A., Furrer H., et al. Hypogonadism in HIV 1-infected men is common and does not resolve during antiretroviral therapy. Antiviral Therapy 2007; 12:261 – 265.