

# Factors associated with reduced bone mineral density (BMD) in HIV-infected patients, ANRS CO 3 Aquitaine Cohort, France

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## Background

Accelerated bone mass loss (osteopenia and osteoporosis) have recently been described in HIV-infected patients. Underlying mechanisms leading to these complications are thought to be multifactorial.

## Objective

To estimate the prevalence of bone abnormalities and investigate factors associated with.

## Methods

We conducted a cross-sectional survey within a cohort of HIV-infected patients. Patients were consecutively enrolled between November 2004 and May 2005. Bone Mineral Density (BMD) of total body, lumbar spine and femoral neck was measured by dual energy x-ray absorptiometry (DEXA). Analyses were stratified according to gender. A multivariable model using polytomous logistic regression was performed.

## Results

492 patients (72.4% male) were recruited (tables 1). Median age was 43 years (Interquartile Range [IQR]: 38-50). 97 (19.7%) patients were at the AIDS stage; 140 (28.5%) had lipodystrophy. Based on World Health Organization (WHO) criteria, osteopenia was diagnosed in 267 (54.3%) patients (table 2) (55.6% of men and 50.7% of women), and osteoporosis in 125 (25.4%) patients (31.5% of men and 9.6% of women).

The multivariable logistic regression showed that older age, HIV transmission group, body mass index, HIV viral load and AIDS were associated with bone abnormalities diagnosis in men (table 3), whereas older age and low CD4+ count nadir were identified in women (table 4).

Table 2: Median T-score [IQR] according to gender, site and patients' diagnosis category, ANRS CO 3 Aquitaine Cohort, France

		No abnormality T-scores>1 (n=100)	Osteopenia -2.5<=T-score<=-1 (n=267)	Osteoporosis T-scores<=-2.5 (n=125)
Total body	men	0.8 [0.4; 1.3]	-0.5 [-1.0; 0.1]	-1.8 [-2.6; -1.2]
	women	0.6 [0.2; 1.3]	-0.6 [-1.1; 0.1]	-2.0 [-2.7; -1.7]
Femoral neck	men	-0.5 [-0.7; 0.0]	-1.9 [-2.3; -1.5]	-3.0 [-3.3; -2.7]
	women	-0.1 [-0.6; 0.3]	-1.4 [-1.8; -1.0]	-2.3 [-2.9; -2.0]
Lumbar spine	men	0.5 [0.0; 1.1]	-0.7 [-1.2; -0.1]	-1.6 [-2.4; -1.1]
	women	0.5 [0.0; 1.1]	-0.9 [-1.6; -0.2]	-2.6 [-2.8; -2.0]

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Tables 1: Patients characteristics according to patients' gender and diagnosis category, ANRS CO 3 Aquitaine Cohort, France

MEN Characteristics (n=356)	No Abnormality		Osteopenia		Osteoporosis	
	% or Median (IQR)	% or Median (IQR)	% or Median (IQR)	% or Median (IQR)		
Prevalence	46 (12.9)	198 (55.6)	112 (31.5)			
Age	41.0 (35.0-48.0)	43.0 (39.0-49.0)	45.0 (40.0-53.5)			
Transmission group						
homosexuality	44.4	59.0	61.5			
heterosexuality	24.4	19.5	15.6			
intravenous drug use	15.6	11.8	15.6			
other	15.6	9.7	7.3			
Follow-up since diagnosis (years)	9.6 (3.5-14.1)	11.0 (6.2-15.4)	11.8 (7.3-15.2)			
AIDS	8.7	23.7	23.2			
Body mass index<20.6 Kg/m <sup>2</sup>	8.7	12.4	35.5			
Lipodystrophy						
lipoatrophy	4.4	9.6	18.7			
fat accumulation	6.5	6.1	3.6			
mixed syndrom	8.7	8.1	15.2			
no abnormality	80.4	76.2	62.5			
CD4+ count<200 /mL	15.2	7.6	9.8			
CD4+ nadir/100cells (/mL)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)			
HIV viral load<500 copies/mL	60.9	72.7	76.8			
NRTI cumulative duration (months)	45.0 (12.1-87.7)	73.7 (33.0-98.3)	78.4 (35.6-103.3)			
NNRTI cumulative duration (months)	3.0 (0.0-21.4)	8.7 (0.0-31.7)	7.0 (0.0-30.5)			
PI cumulative duration (months)	3.0 (0.0-32.9)	22.9 (0.0-52.1)	27.6 (0.0-49.1)			

IQR: interquartile range; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: non nucleoside reverse transcriptase inhibitor; PI: protease inhibitor

Table 3: Factors associated with osteopenia and osteoporosis in HIV positive men (n=298), compared to those without bone abnormality (n=45), ANRS CO 3 Aquitaine Cohort, France

	Osteopenia (n=191)		Osteoporosis (n=107)	
	OR [95%CI]	p-value	OR [95%CI]	p-value
Age (by 10 years)	1.34 [0.91; 1.96]	0.14	2.14 [1.40; 3.26]	5.10 <sup>-4</sup>
Transmission group				
homosexuality	1.00	0.10	1.00	5.10 <sup>-4</sup>
heterosexuality	0.50 [0.21; 1.17]		0.33 [0.12; 0.90]	
intravenous drug use	0.46 [0.17; 1.26]		0.46 [0.15; 1.39]	
other	0.29 [0.10; 0.87]		0.12 [0.04; 0.44]	
Body mass index<20.6 Kg/m <sup>2</sup>	2.49 [0.74; 8.41]	0.14	14.68 [4.20; 51.29]	<10 <sup>-4</sup>
HIV viral load<500 copies/mL	2.06 [1.01; 4.18]	0.05	3.19 [1.40; 7.29]	6.10 <sup>-3</sup>

OR: Odds ratio; CI: Confidence interval

WOMEN Characteristics (n=136)	No Abnormality		Osteopenia		Osteoporosis	
	% or Median (IQR)	% or Median (IQR)	% or Median (IQR)	% or Median (IQR)		
Prevalence	54 (39.7)	69 (50.6)	13 (9.6)			
Menopause	13.0	24.6	53.8			
Age	39.0 (34.0-43.0)	42.0 (39.0-47.0)	58.0 (46.0-67.0)			
Transmission group						
heterosexuality	75.5	67.2	41.7			
intravenous drug use	18.4	20.9	25.0			
other	6.1	11.9	33.3			
Follow-up since diagnosis (years)	10.8 (5.2-14.4)	12.6 (8.4-15.7)	14.8 (9.3-16.0)			
AIDS	9.3	18.8	15.4			
Body mass index<20.6 Kg/m <sup>2</sup>	34.0	39.4	53.8			
Lipodystrophy						
lipoatrophy	3.7	7.2	38.5			
fat accumulation	11.1	8.7	7.7			
mixed syndrom	7.4	17.4	7.7			
no abnormality	77.8	66.7	46.1			
CD4+ count<200 /mL	9.3	7.2	15.4			
CD4+ nadir/100cells (/mL)	2.0 (2.0-4.0)	2.0 (1.0-3.0)	1.5 (0.5-3.0)			
HIV viral load<500 copies/mL	64.8	72.5	84.6			
NRTI cumulative duration (months)	61.5 (25.9-101.9)	77.2 (37.2-107.0)	77.6 (33.2-112.2)			
NNRTI cumulative duration (months)	1.8 (0.0-23.8)	11.6 (0.0-31.2)	25.7 (15.3-53.3)			
PI cumulative duration (months)	3.0 (0.0-20.3)	18.4 (0.0-65.1)	20.6 (0.0-68.5)			

IQR: interquartile range; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: non nucleoside reverse transcriptase inhibitor; PI: protease inhibitor

Table 4: Factors associated with osteopenia and osteoporosis in HIV positive women (n=79), compared to those without bone abnormality (n=49), ANRS CO 3 Aquitaine Cohort, France

	Osteopenia or Osteoporosis (n=79)	
	OR [95%CI]	p-value
Age (by 10 years)	1.69 [1.10; 2.59]	0.02
CD4+ count nadir (/mL)	0.70 [0.54; 0.91]	8.10 <sup>-3</sup>

OR: Odds ratio; CI: Confidence interval

## Conclusion

These data showed a high prevalence of osteopenia and osteoporosis in our cohort. The multifactorial hypothesis is substantiated by the associations found. Mechanisms (including treatment exposure) and consequences of these bone disorders need to be further explored.