

Reduced Bone Mineral Density in HCV- or HBV-co-infected patients: two- years follow-up, ANRS CO3 Aquitaine Cohort, France

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Background

A high prevalence of bone demineralization among HIV-infected patients has been already reported. A previous survey within the Aquitaine cohort among 363 HIV-mono-infected patients showed that osteopenia was diagnosed in 53.4% of men (95% confidence interval (CI): 47.4-59.4%) and 50.5% of women (CI: 40.6-60.3%) and osteoporosis in 34.5% of men (CI: 28.8-40.2%) and 7.1% of women (CI: 0.02-12.2%). Chronic viral hepatopathy is a risk factor of bone demineralization. Little is known about the temporal changes of bone abnormalities in HIV-infected patients. We examined the two-year progression of bone mineral density (BMD) and body composition in a cohort of HIV-infected patients and we estimated the prevalence of osteoporosis/osteopenia according to the hepatitis co-infection status.

Methods

Patients were consecutively screened for BMD and hepatitis co-infection in November 2004-May 2005. Two years later, we repeated the BMD assessment in patients who had no bone abnormality or diagnosed with osteopenia at baseline, osteoporotic patients (N=132) were excluded (WHO criteria). We expanded in 2007 the enrolment of hepatitis co-infected patients to estimate the BMD prevalence in this group. Hepatitis co-infected patients were patients with current or past HCV infection or with chronic HBV infection, defined by the positivity of plasma HBs antigen. BMD of whole body, lumbar spine and femoral neck was measured by Dual Energy X-ray Absorptiometry (DEXA) as well as bone mineral content, fat and lean body mass.

Results

Two hundred and eight patients were repeatedly assessed in the longitudinal study (67.8% male; median age: 46 years, Interquartile Range [IQR]: 41-53; 26.7% with normal BMD and 73.3% with osteopenia at baseline). After 2 years, 39 patients (18.7%) remained free of bone abnormality; osteopenia was diagnosed in 147 patients (70.7%) and osteoporosis in 22 (10.6%). Osteopenia predominated at the femoral neck in both men and women and osteoporosis at the femoral neck in men (Table 1). A fat mass significant decline (median -2.9%) was observed in those acquiring osteopenia compared to those remaining normal (+7.5%) ($p = 0.01$). Osteopenic patients at baseline presented a significant femoral neck BMD decline when becoming osteoporotic (-4.2%) compared to those who remained osteopenic (-1.9%) ($p = 1.2 \cdot 10^{-3}$).

Table 1. Median T-score [IQR] according to gender, site and patients' diagnosis at 24-months, ANRS CO3 Aquitaine Cohort, France

Total		No abnormality	Osteopenia	Osteoporosis
		T-score>-1	-2.5<=T-score<=-1	T-score<=-2.5
N=208 (100%)		N=39 (18.7%)	N=147 (70.7%)	N=22 (10.6%)
Whole body	Male	0.0 [-0.4;0.5]	-0.9 [-1.5;-0.2]	-1.5 [-1.9;-0.7]
	Female	0.4 [-0.1;1.5]	-0.9 [-1.6;-0.4]	-2.9 [-3.5;-2.0]
Femoral neck	Male	-0.6 [-0.7;-0.3]	-2.0 [-2.2;-1.5]	-2.7 [-2.8;-2.6]
	Female	-0.4 [-0.6;-0.1]	-1.3 [-1.9;-1.0]	-2.6 [-2.6;-2.2]
Lumbar spine	Male	1.2 [0.8;1.5]	-0.4 [-0.8;0.1]	-1.0 [-1.4;-0.8]
	Female	0.7 [0.1;1.9]	-0.3 [-0.9;0.2]	-1.4 [-1.6;-1.2]

Table 2. Median percentage of variation [IQR] in BMD and body composition after 24 months, ANRS CO3 Aquitaine Cohort, France

Baseline diagnosis	No abnormality (N=54)			Osteopenia (N=154)		
	No	Osteopenia	p^{*1}	Osteopenia	Osteoporosis	p^{*2}
24-months diagnosis	N=39 (72.2%)	N=15 (27.8%)		N=132 (85.7%)	N=22 (14.3%)	
Whole body BMD	-0.4 [-1.4;0.9]	-0.5 [-2.2;-0.1]	0.26	0.0 [-1.6;1.2]	-0.2 [-1.4;0.8]	0.49
Femoral neck BMD	-2.0 [-5.3;0.4]	-4.6 [-6.0;-2.3]	0.12	-1.9 [-4.5;0.4]	-4.2 [-6.8;-1.8]	1.2.10³
Lumbar spine BMD	-0.1 [-3.9;1.9]	-1.9 [-3.0;-0.5]	0.30	-0.1 [-2.1;2.4]	-1.6 [-4.9;3.7]	0.57
Fat mass	7.5 [0.4;25.2]	-2.9 [-12.3;4.3]	0.01	9.2 [-2.1;21.3]	7.1 [-1.3;22.3]	0.84
Lean mass	0.7 [-1.8;3.0]	-0.7 [-3.4;4.0]	0.18	-0.3 [-2.6;1.6]	-2.1 [-4.1;-0.7]	0.07

*1 Comparison no abnormality versus osteopenia; *2 comparison osteopenia versus osteoporosis

BMD was investigated in 85 hepatitis co-infected patients (76.5% HCV, 20.0% HBV, 3.5% both; 71.8% male; median age 45 years ([IQR]: 42-48); 28.2% AIDS stage; 88.2% treated by highly active antiretroviral therapy (HAART); 12.9% with cirrhosis) (Tables 3). Prevalence of osteopenia was 52.5% in men (CI: 40.0-65.0%), and 58.4% among women (CI: 38.6-78.0%). Osteoporosis was diagnosed in 34.4% of men (CI: 22.5-46.3%) and 8.3% of women (CI: 2.7-19.3%). These prevalence estimates of bone demineralization were not statistically different from those documented in HIV-alone patients two years earlier.

Tables 3. Co-infected patients characteristics according to the gender and the diagnostic categories of BMD, ANRS CO3 Aquitaine Cohort, France

CO-INFECTED MEN characteristics	Total	No abnormality	Osteopenia	Osteoporosis
	% or median [IQR]	% or median [IQR]	% or median [IQR]	% or median [IQR]
N=61 (100%)	100	13.1	52.5	34.4
Age (years)	45.0 [43.0-48.0]	44.5 [42.5-45.5]	47.0 [43.5-49.0]	45.0 [42.0-47.0]
Follow-up since HIV diagnosis (years)	17.5 [14.7-19.6]	16.5 [11.6-19.5]	17.0 [13.3-20.0]	18.3 [16.3-19.7]
AIDS clinical stage	27.9	---	37.5	23.8
HAART-treated	91.8	75.0	96.9	90.5
HCV co-infected	77.0	100.0	75.0	71.4
Cholestasis	55.3	75.0	45.8	60.0
Plasma HCV RNA positive	70.2	50.0	70.8	80.0
Genotype 1 or 4	55.6	50.0	58.8	50.0
Genotype 2 or 3	44.4	50.0	41.2	50.0
Cirrhosis stage	17.0	25.0	12.5	20.0
HBV co-infected	27.9	12.5	25.0	38.1
Cholestasis	52.9	---	62.5	50.0
Cirrhosis stage	11.8	---	12.5	12.5

CO-INFECTED WOMEN characteristics	Total	No abnormality	Osteopenia	Osteoporosis
	% or median [IQR]	% or median [IQR]	% or median [IQR]	% or median [IQR]
N=24 (100%)	100	33.3	58.4	8.3
Age (years)	44.0 [42.0-46.0]	43.5 [40.0-46.0]	44.0 [43.0-49.0]	42.0 [42.0-42.0]
Follow-up since HIV diagnosis (years)	18.9 [15.6-21.1]	17.7 [11.6-20.7]	18.9 [15.7-21.2]	19.8 [17.7-21.8]
AIDS clinical stage	29.2	12.5	28.6	100.0
HAART-treated	79.2	87.5	78.6	50.0
HCV co-infected	87.5	87.5	85.7	100.0
Cholestasis	40.0	33.3	33.3	100.0
Plasma HCV RNA positive	76.2	71.4	75.0	100.0
Genotype 1 or 4	53.3	60.0	37.5	100.0
Genotype 2 or 3	46.7	40.0	62.5	---
Cirrhosis stage	4.8	14.3	---	---
HBV co-infected	12.5	12.5	14.3	---
Cholestasis	33.3	---	100.0	---
Cirrhosis stage	---	---	---	---

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Conclusion

This study confirms our earlier findings of a high prevalence of bone mineral disorders in HIV patients. However, we did not observe any association with viral hepatitis co-infection. Bone metabolism is rapidly evolving in two years among HIV-infected patients and underlying biological mechanisms need further investigation.